Radiology in the Diagnosis and Treatment Monitoring of Pediatric Sarcoma

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Rhabdomyosarcoma of Genitourinary tract

- Rhabdomyosarcoma is the **most common pediatric soft-tissue sarcoma** .
- The head and neck, genitourinary tract, and extremities are the most prevalent locations.
- The median age at diagnosis is 5 years .
- Approximately 40% of these tumors originate in the pelvis, including the bladder, prostate, paratesticular tissues, vagina, uterus, and cervix

Demographics

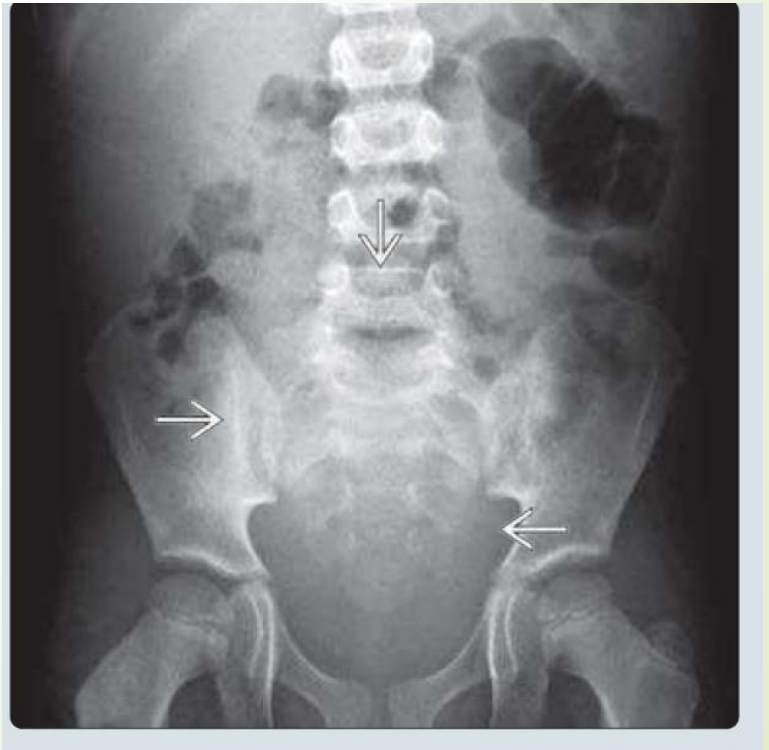
- Age
  - **Peak incidence: 2-6 years old**
  - 75% < 5 years old at diagnosis
  - Paratesticular tumors are more common in adolescents
- Sex
  - M:F = 2-3:1 for GU tumors
  - M = F for head, neck, & extremity tumors
- Epidemiology
  - 250 new cases per year in USA
  - 4.5 cases per million

Rhabdomyosarcoma

- Embryonal cell type has better prognosis than alveolar
- RMS of paratesticular tissues & vas deferens have best prognoses
- 15-20% have metastases at diagnosis

Imaging Findings

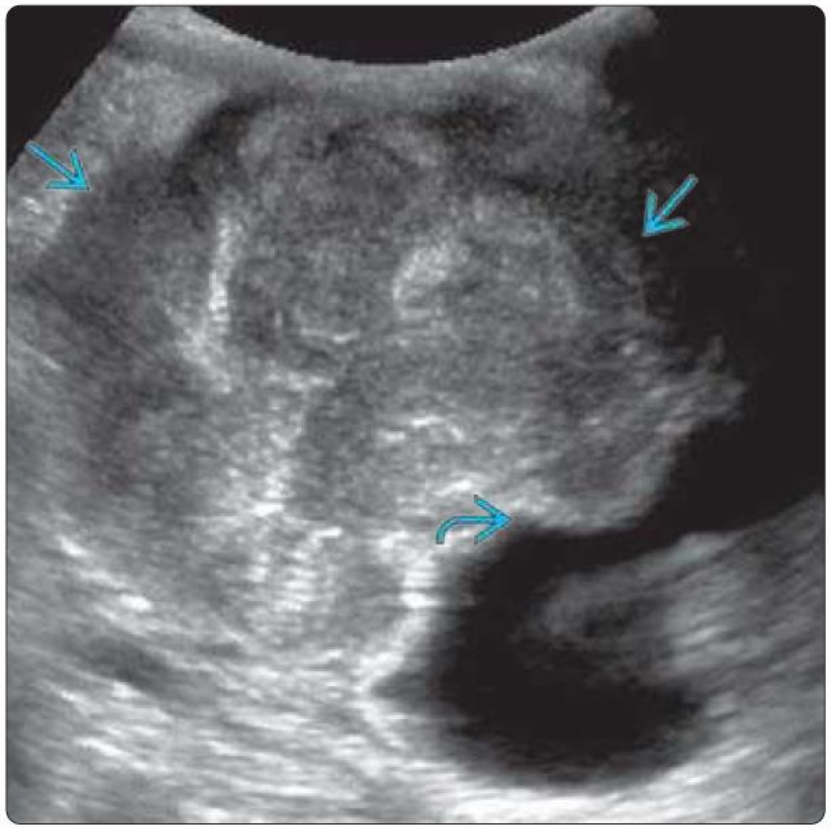
- **Radiography: Soft tissue mass displacing bowel out of pelvis; can mimic distended urinary bladder**

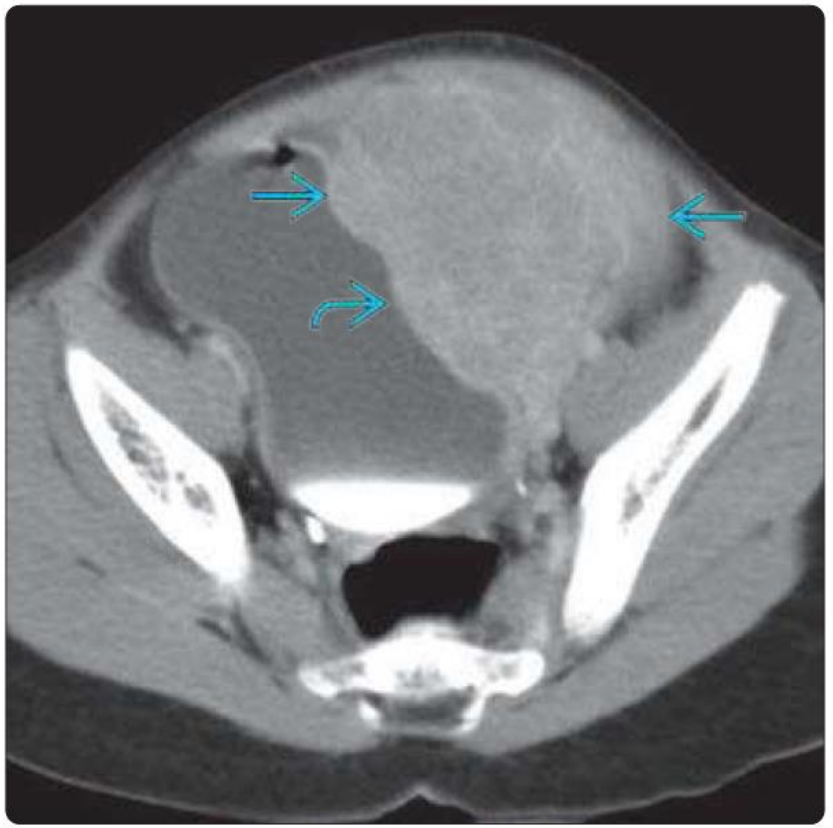


Ultrasonographic Findings

- Grayscale ultrasound
  - Round or lobulated tumor distorting &/or extending into urinary bladder
  - Mass is typically large & heterogeneous
  - Most commonly solid with variable cystic components
  - Look for evidence of urinary tract obstruction & adenopathy

- Color Doppler
  - Internal vascularity is variable in degree
  - Useful to trace displaced & compressed vessels
  - Vascular invasion is unusual

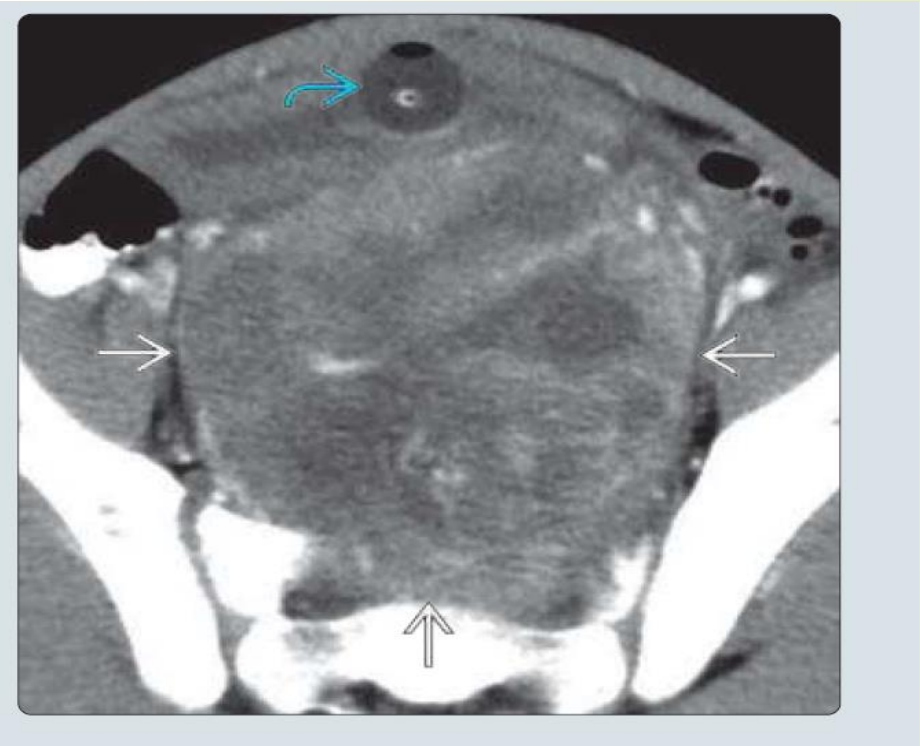




(Left) *Longitudinal US in a 4-year-old girl shows a lobulated, heterogeneous mass ⇨ distorting the anterior wall ⇗ of the urinary bladder. Vascularity in the mass on color Doppler (not shown) confirmed a solid lesion.* **(Right)** *Axial CECT of the pelvis in the same patient shows the enhancing mass ⇨ involving the lateral wall ⇗ of the urinary bladder. Biopsy confirmed RMS.*

CT Findings

- CECT
  - Heterogeneously enhancing, predominantly solid mass
  - Frequently locally invasive; look for disruption of fat planes
  - Search for adjacent adenopathy
  - Include liver due to frequency of metastatic disease



MR Findings

- Intermediate to low T1, intermediate to high T2 signal intensity
- Variable degrees of enhancement, ranging from mild & heterogeneous to intense & uniform

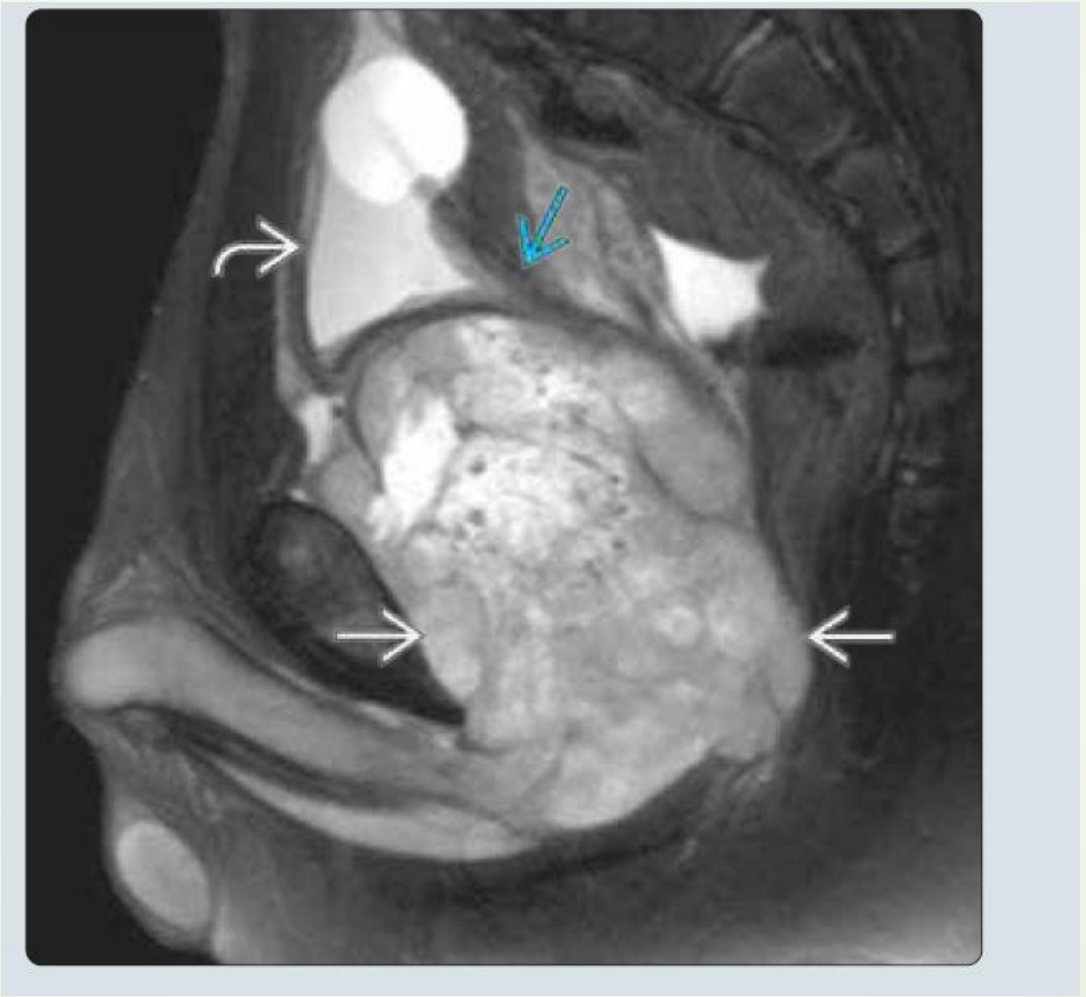
• DWI

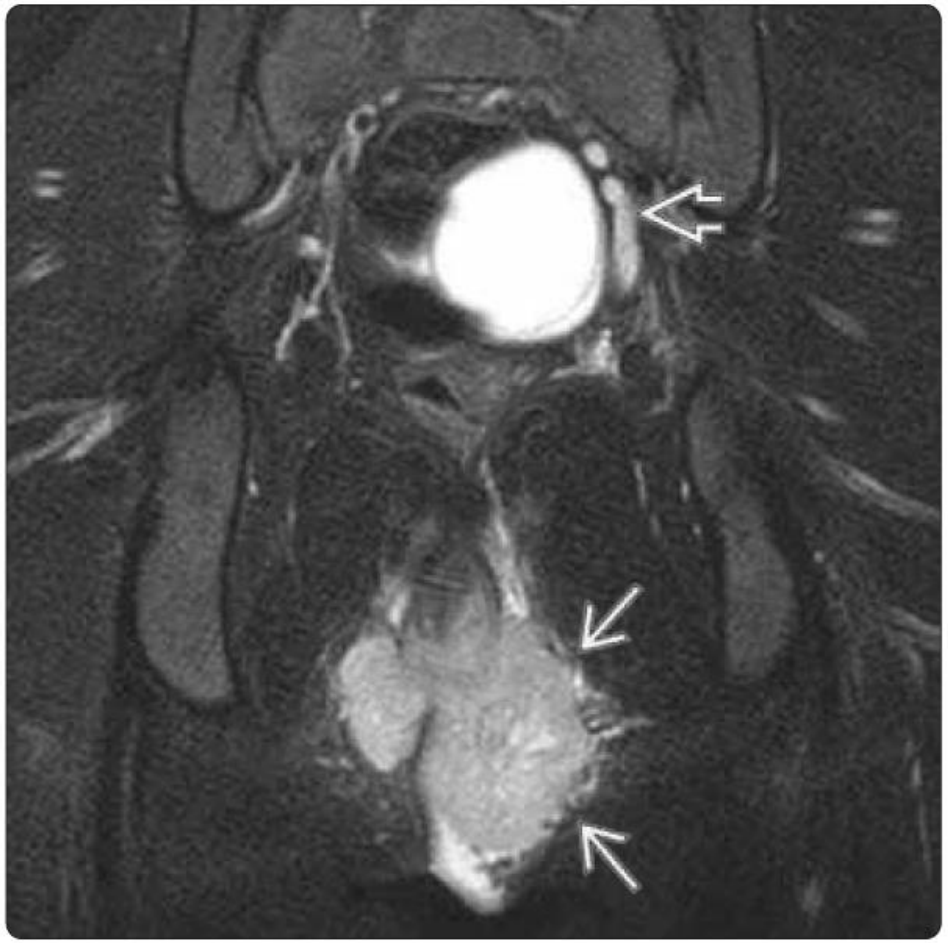
- Solid portions of tumor typically restrict diffusion
- DWI ↑ conspicuity of all lymph nodes (normal & pathologic), helping draw attention to mildly enlarged nodes that might otherwise go unnoticed

Modality of choice for tumor evaluation

- Because **MRI** has superior contrast resolution, it is the preferred modality in evaluating soft-tissue sarcomas.
- It provides the most detailed characterization of the tumor and surrounding tissues. It is imperative that the **MRI field of view includes local lymph nodes and locoregional disease extension**

Sagittal
T2 FS MR in a 7-year-old boy shows a large, heterogeneous, high signal intensity RMS arising from the prostate. Note the superior displacement of the bladder & the altered course of the catheter .





irregular high signal intensity mass in the left labia ft of this 15-year-old girl, initially treated as infection. Subsequent biopsy showed RMS. Suspicious left-sided lymph nodes are seen in the iliac chain.

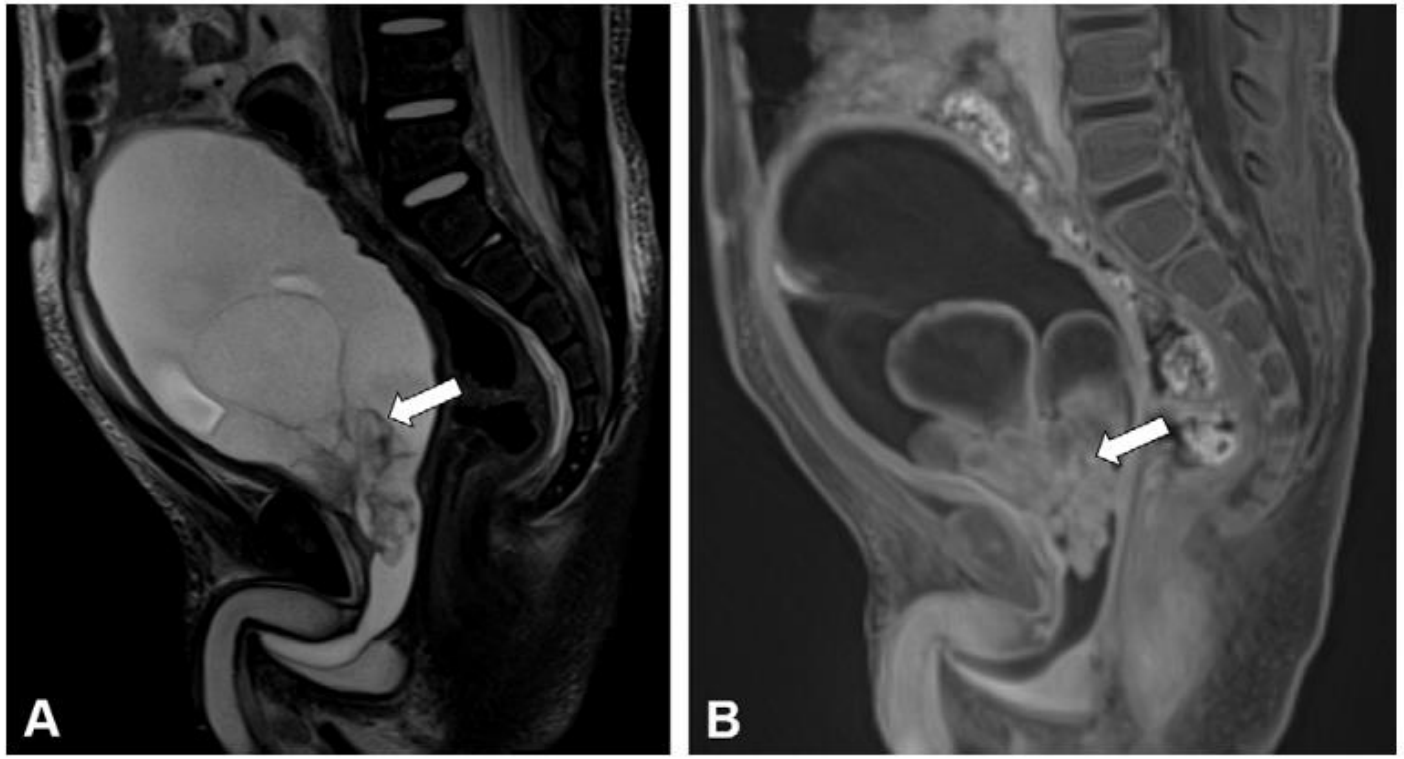


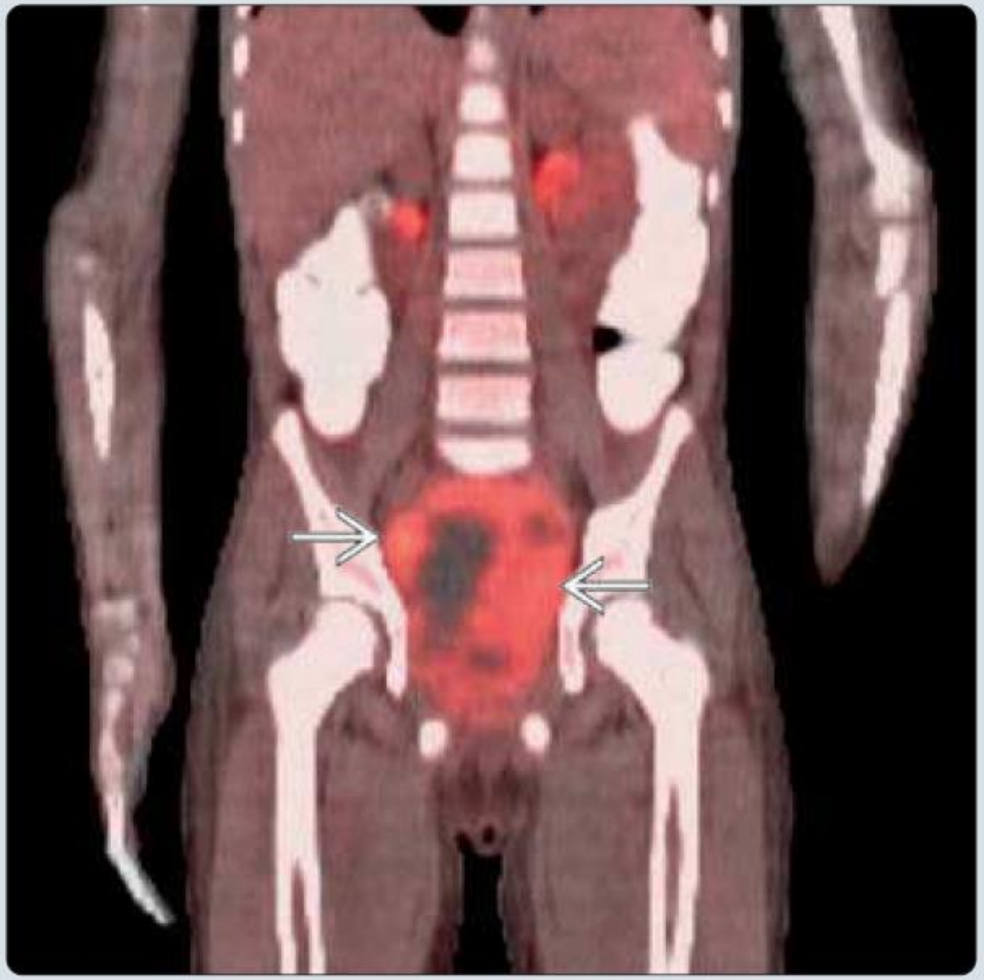
Figure 35. Urinary bladder base botryoid embryonal rhabdomyosarcoma in a 3-year-old patient. Sagittal T2-weighted **(A)** and postcontrast fat-saturated T1-weighted **(B)** MR images show a polypoid grapelike lesion (arrow) centered at the urinary bladder base.

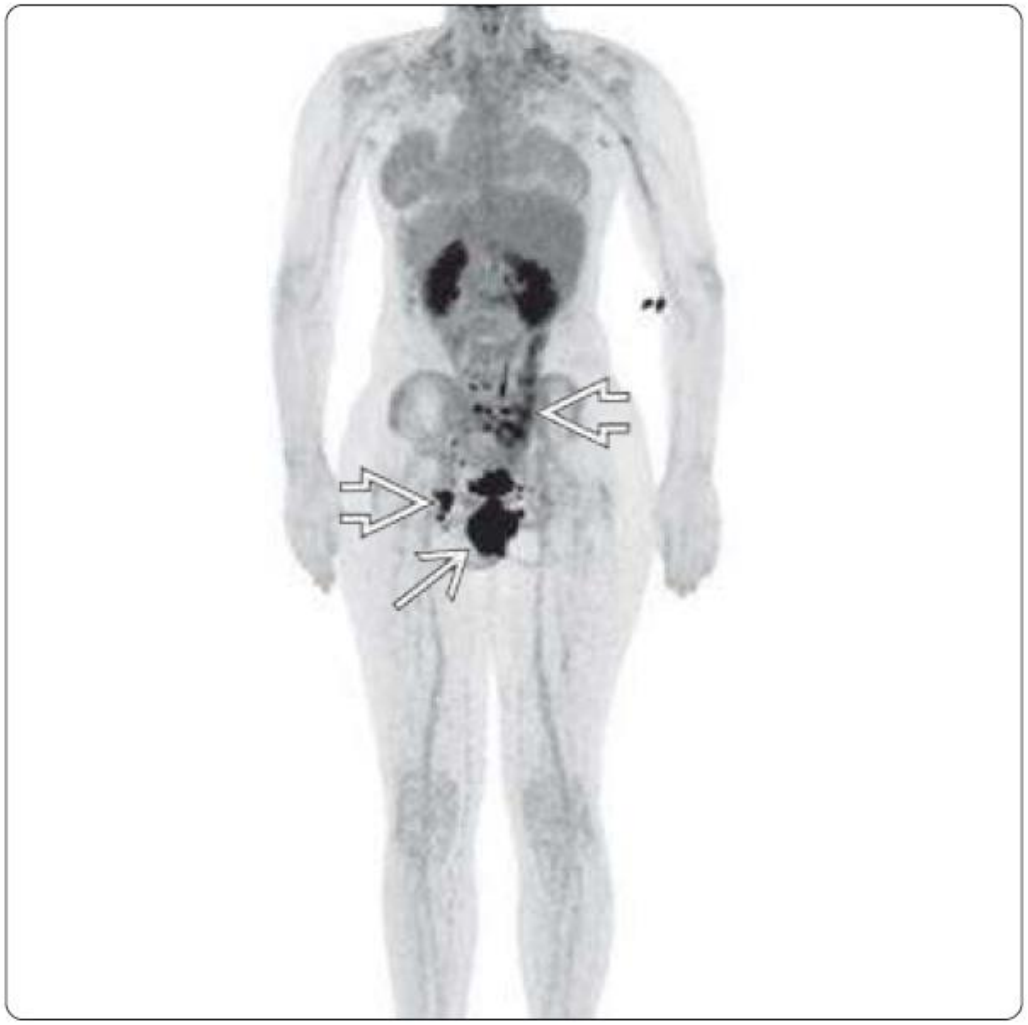
Nuclear Medicine Findings

- Bone scan
  - Traditionally used for bony metastatic disease

- PET/CT
  - Improves staging with ↑ sensitivity for nodal spread & distant metastases
  - May improve assessment of therapeutic response

(Left) *Coronal FDG PET/CT in the same patient shows predominantly peripheral uptake in the pelvic tumor* ➔ *but no evidence of metastatic disease. Biopsy confirmed a rhabdomyosarcoma (RMS) originating from the bladder base/prostate.* **(Right)** *Sagittal T2 FS MR in a 7-year-old boy shows a large, heterogeneous, high signal intensity RMS* ➔ *arising from the prostate. Note the superior displacement of the bladder* ➔ *& the altered course of the catheter* ➔.





(Left) *Coronal T2 FS MR shows irregular high signal intensity mass in the left labia ➔ of this 15-year-old girl, initially treated as infection. Subsequent biopsy showed RMS. Suspicious left-sided lymph nodes ➔ are seen in the iliac chain.* **(Right)** *Posterior view 3D MIP FDG PET in the same patient shows that the primary tumor is FDG avid ➔ & that FDG-avid lymph nodes are present bilaterally in the groin & pelvis ➔.*

Imaging Recommendations

- Best imaging tool
- **US** is typically used for initial investigation of urinary tract symptoms or palpable mass
- **CECT or MR** for further tumor characterization & localization
- Staging with **chest CT & PET**

BX Key Principles

- After appropriate imaging assessment, the standard approach to diagnosis of RMS, consists of multiple image-guided (ultrasound whenever possible) core needle biopsies, preferably with a 16 gauge or larger needle.
- The biopsy should be carried out at large referral centers by experienced interventional radiologists or surgeons after multidisciplinary discussion. The interventional radiologist should be aware that the biopsy tract and subsequent scar must be resected during definitive surgery because of the potential for tumor cell seeding

BX

- Biopsy is indicated when:

1. **Diagnosis is uncertain**
    1. Imaging alone cannot reliably distinguish RMS from other GU tumors (e.g., urothelial carcinoma, sarcomatoid tumors, lymphoma).
2. **Before starting systemic therapy**
    1. Histopathologic confirmation is required before chemotherapy or radiation.
3. **Surgical planning**
    1. To guide the extent of resection or organ-sparing procedures.
    2. Helps in **risk stratification** according to histologic subtype (embryonal vs alveolar).
4. **Unresectable tumors at presentation**
    1. If the tumor is locally advanced and initial surgery is not feasible, biopsy provides tissue for neoadjuvant chemotherapy.
5. **Suspected metastatic disease**
    1. Tissue confirmation may be required if distant lesions are accessible for biopsy.

- **Preferred methods:**

- **Core needle biopsy** (percutaneous, image-guided) is generally preferred.
- **Open incisional biopsy** may be used if needle biopsy is not feasible.
- **Avoid transurethral biopsy of bladder/prostate** unless no other approach exists, because it may compromise future surgery or staging.

Bx

- **Contraindications**

1. **Risk of tumor spillage or seeding**
    1. Avoid biopsy routes that traverse uninvolved tissue planes that might be included in future resection.
    2. Example: perineal biopsy of paratesticular or prostate tumors may increase local recurrence risk.
2. **Uncorrectable coagulopathy or high bleeding risk**
    1. Biopsy should be postponed until coagulation status is optimized.
3. **Inaccessible tumors without safe biopsy route**
    1. Risk to vital structures (e.g., large pelvic vessels) may outweigh benefit.
4. **Obvious resectable mass in an organ-sparing site** (controversial)
    1. In some GU RMS (e.g., small paratesticular tumors), upfront excision with sentinel node assessment may be preferred

DIFFERENTIAL DIAGNOSIS

Ureterocele

- Cystic protrusion of distal ureter into bladder; ureteral jet &/or continuity with dilated ureter can help confirm

Bladder Hematoma/Debris

- Clinical history of instrumentation, augmentation, trauma, cystitis, or chemotherapy
- Heterogeneous mobile filling defect(s); no Doppler flow

Pelvic Neuroblastoma

- Younger age, Ca^{2+}, & encasement of vessels

Burkitt Lymphoma

- Look for bowel, splenic, & renal involvement

Ovarian Tumor

- Identifying organ of origin may be difficult
- Ovarian malignancies are often larger with higher likelihood of peritoneal spread (nodules, ascites)

Hematometrocolpos

- Markedly distended vagina posterior to bladder
- Look for layering or swirling debris on US
- Blood products are often bright on T1 MR

Sacrococcygeal Teratoma

- Heterogeneous solid &/or cystic presacral mass associated with coccyx
- Most commonly exophytic from perineum in newborn with variable size of internal components

Rhabdomyosarcoma Staging

- Three key pieces of information are necessary to divide patients into risk groups, which guide treatment:

1- the TNM stage

2- the clinical group (based on the extent of disease removal during the initial surgery)

3- and the presence of the PAX3/FOX01 or PAX7/FOX01 fusion gene (patients with fu sion-positive tumors have a poorer prognosis)

Stage	Organ	Tumor (T)	Size	Lymphnode (N)	Metastases (M)
I	Paratesticular, vaginal uterine	T1 or T2	a, b	N0, N1, Nx	M0
II	Bladder, prostate	T1 or T2	a	N0, Nx	M0
III	Bladder, prostate	T1 or T2	a	N1	M0
	b	N0, N1, Nx			
IV	All	T1 or T2	a, b	N0 or N1	M1

T1, tumor confined to site of origin (a, diameter <5 cm; b, diameter >5 cm).
T2, local infiltration, extension, or adherence (a, diameter <5 cm; b, diameter >5 cm).
N0, negative regional lymph nodes; N1, positive regional lymph nodes.
Nx, lymph nodes status unknown; M0, no distant metastases; M1, positive distant metastases.

Rhabdomyosarcoma Response Assessment

- There are two accepted ways to assess rhabdomyosarcoma treatment response: **RECIST 1.1 or volumetric (three-dimensional).**
- Recent studies suggest that, unless progressive disease occurs, which is associated with a poor prognosis, **the degree of volume response does not guide treatment .**
- In RECIST 1.1, as well as the detection of new lesions, a one-dimensional increase of 20% is considered progressive. This corresponds to a 73% volumetric increase

Measurements of Tumor

- The European Pediatric Soft-Tissue Sarcoma Study Group recommends one-dimensional measurements of pediatric and adolescent rhabdomyosarcomas according to RECIST(Response Evaluation Criteria in Solid Tumors)
- However, three-dimensional measurements can also be performed , as neither method has conclusive superiority to date.

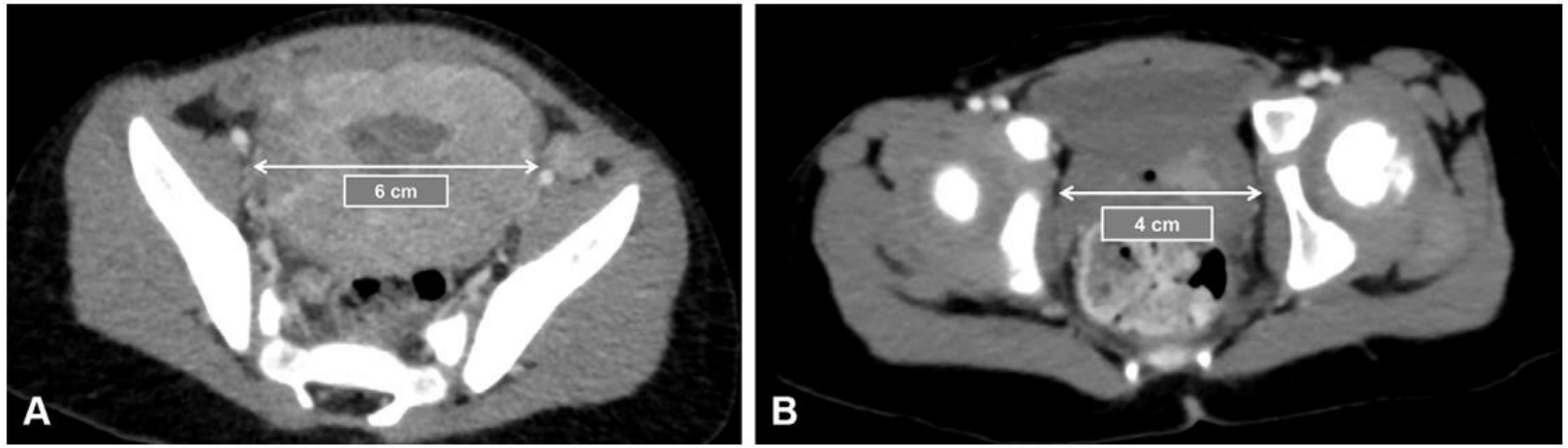
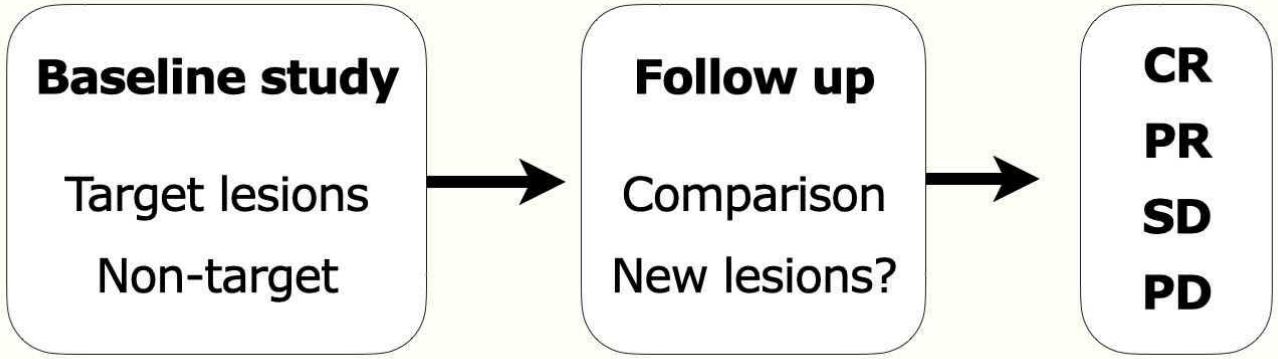
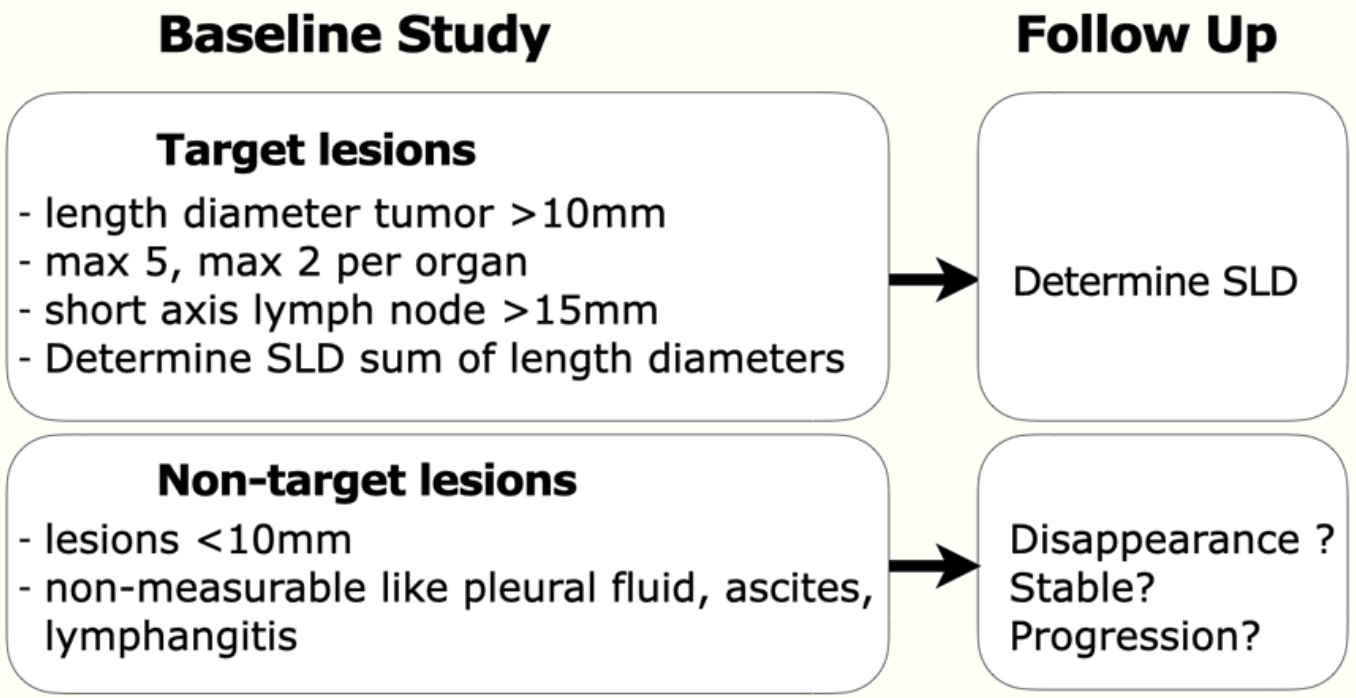


Figure 36. Vaginal rhabdomyosarcoma in a 3-year-old girl who presented with a heterogeneous pelvic mass. Axial contrast-enhanced CT images of the pelvis were obtained before **(A)** and after **(B)** treatment. Double-sided arrow shows the one-dimensional largest measurement method (62). There is a decrease (33%) in size from that at baseline, indicating partial response.

RECIST 1.1



RECIST 1.1



RECIST 1.1

Response

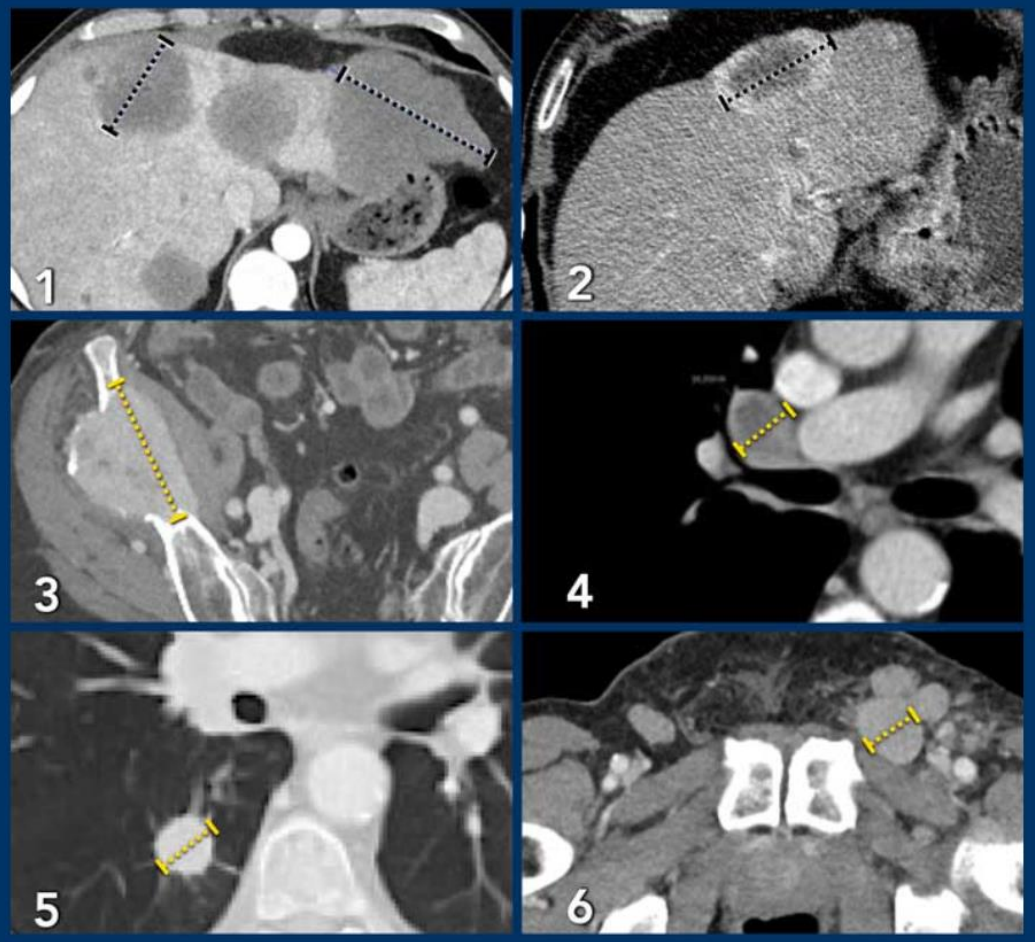
CR Disappearance of all lesions and pathologic lymph nodes

PR ≥ 30% decrease SLD
no new lesions
no progression of non-target lesions

SD no PR - no PD

PD ≥ 20% increase SLD* compared to smallest SLD in study
or progression of non-target lesions
or new lesions

Target lesions



Examples of target lesions

Tumors

Choose preferably large well-described lesions to measure with a longest diameter ≥ 10 mm, a maximum of two per organ and a maximum of five for the whole study.

Lymph nodes

Lymph nodes can be used as target lesions provided that the maximum short axis diameter exceeds 15 mm.

Examples of target lesions:

1. Liver metastases: maximum of 2 measurements per organ.
2. Include hypervascular ring for measurement.
3. Bone metastasis, only soft tissue component is suitable for measurement as target lesion. Sclerotic lesions are not suited for target lesion.
4. Mediastinal lymph node: short axis ⩾ 15mm.
5. Lung metastasis ⩾ 10mm.
6. Inguinal lymph node short axis ⩾ 15mm.

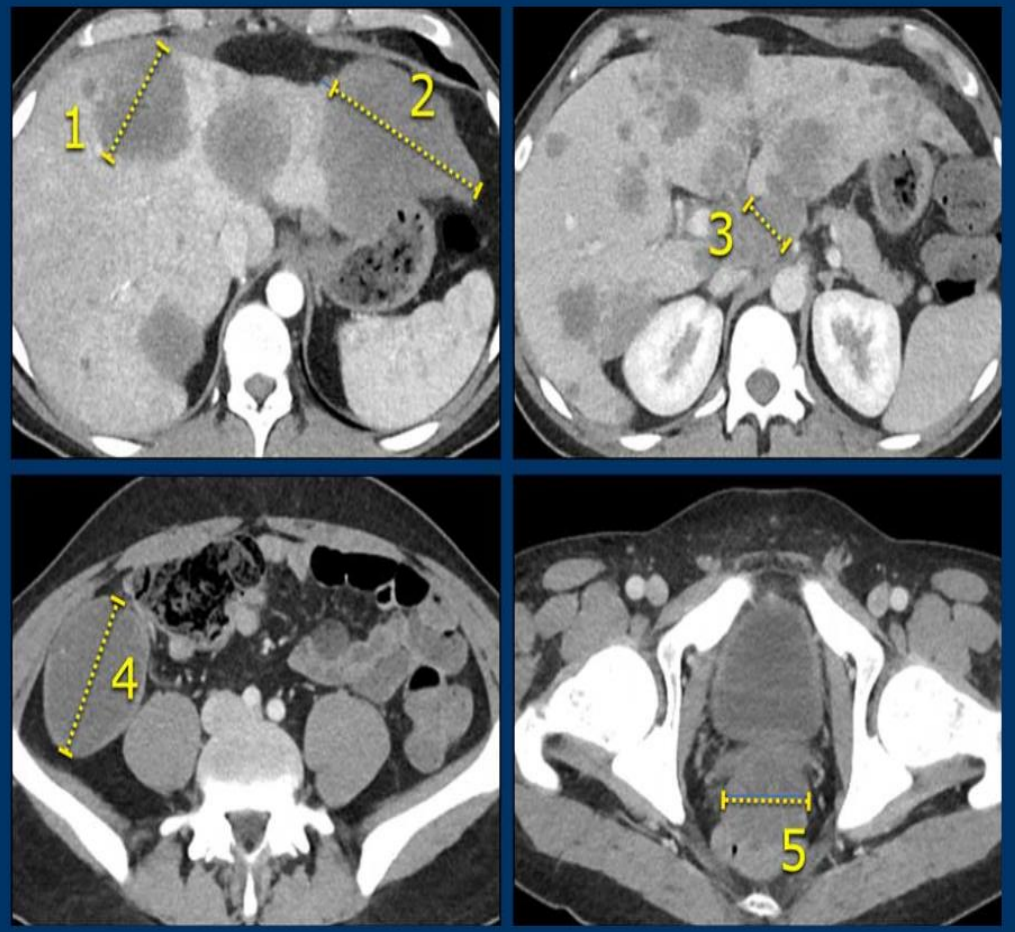
Criteria for target lesions

Tumours	Malignant lymph nodes
CT scan: long axis ⩾ 10mm Chest X-ray: long axis ⩾ 20mm	*Short* axis diameter ⩾ 15mm

Lymph nodes <10 mm are regarded as normal.

Lymph nodes 10-14mm are regarded as pathologic, but not suited for target lesions.
They can be used as non-target lesions.

When target lymph nodes decrease to a normal size (<10 mm), their measurements still have to be included in the sum of the longest diamters (SLD).



Sum of Longest Diameters

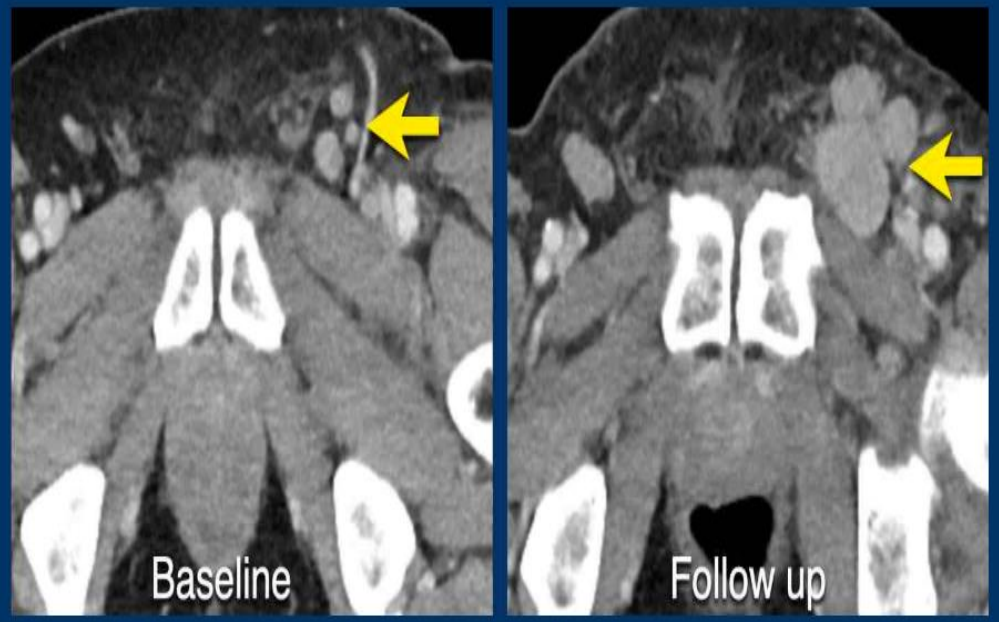
Here an example of a 28-year-old male with a neuroendocrine carcinoma of the appendix.

There are 5 lesions suited for measurement:

- In the liver there are two metastases that are suited for measurement (1 and 2).
- In the porta hepatis there is a lymph node with a short axis > 15mm (3).
- There are two peritoneal metastases (4 and 5).

The SLD = diameter of 1+2+3+4+5.

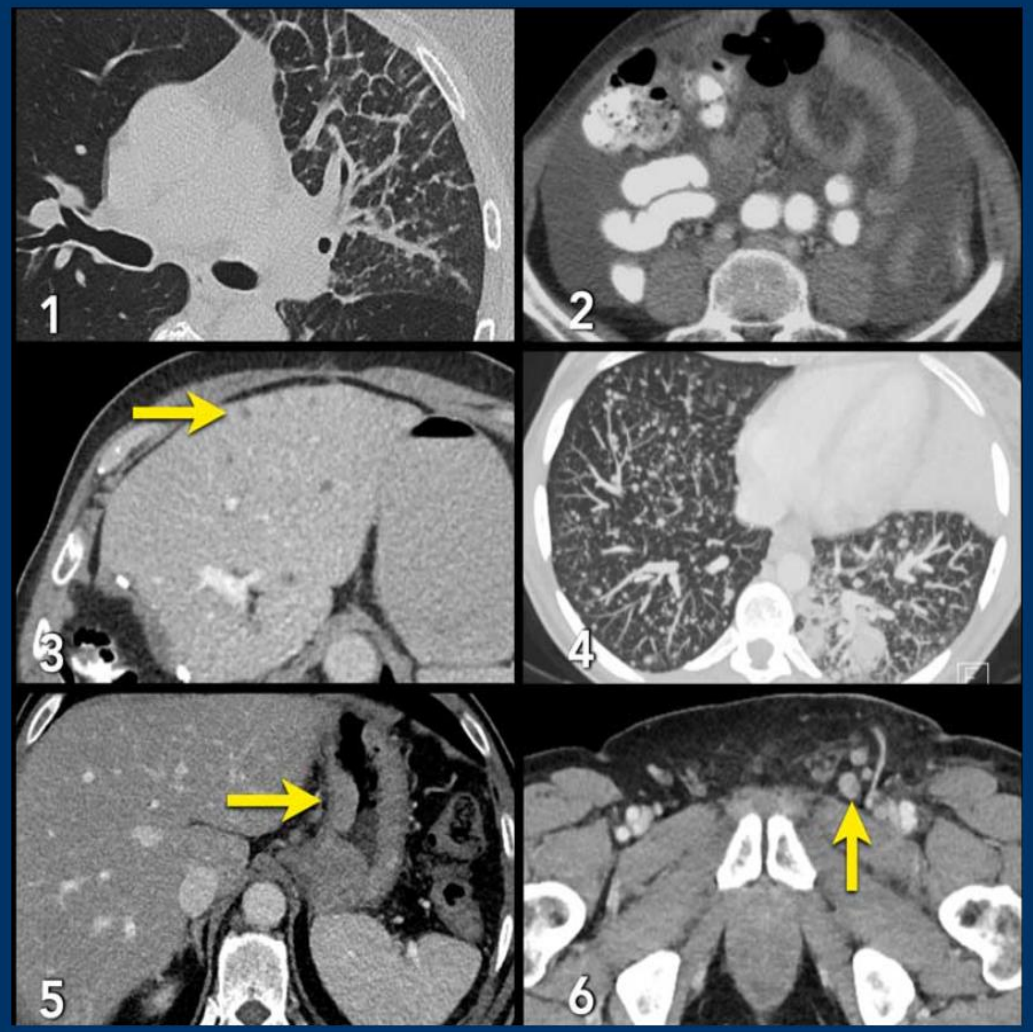
Non-target lesions



During follow up there is unequivocal progression of lymph node metastases, which were choosen as non-target lesions

Non-target lesions are:

- Tumor lesions < 10 mm
- Lymph nodes ≥ 10 -15 mm
- Truly non-measurable disease: eg. leptomeningeal disease, ascites , effusions, inflammatory breast disease, and lymphangitic involvement of skin or lung.
- Any supernumerary lesions that meet the measurability criteria when the maximum number of target lesions has been reached.



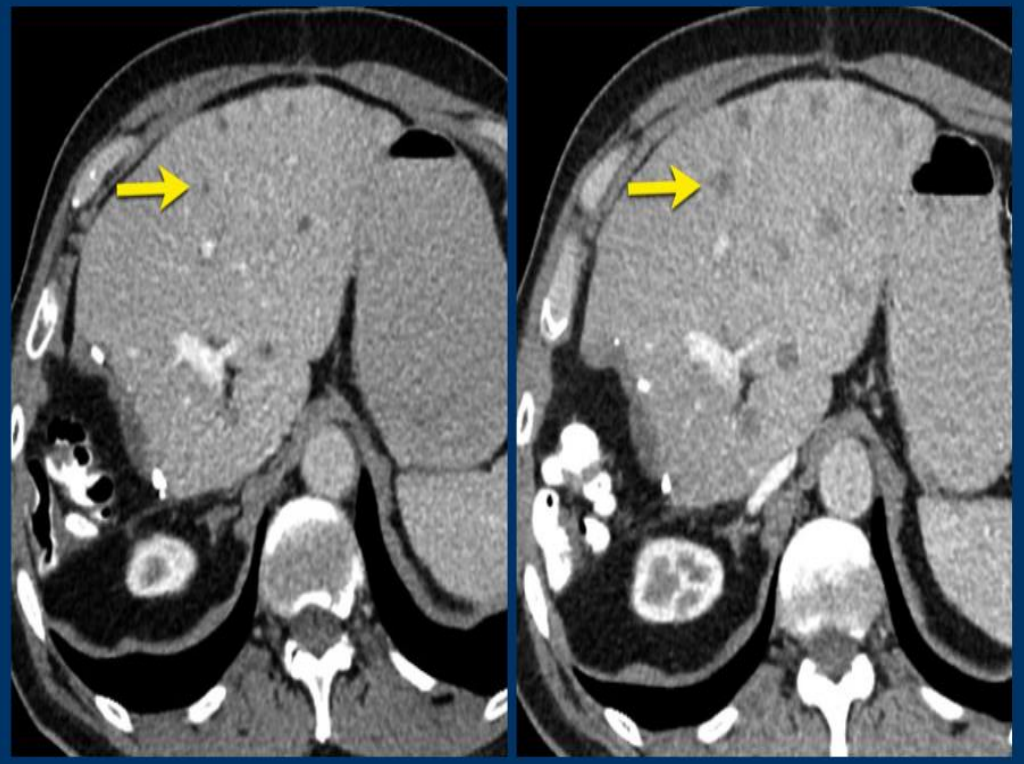
Examples of non-target lesions:

1. Pulmonary lymphangitis carcinomatosa.
2. Ascites.
3. Livermetastases too small for measurement as target lesion, but can be used as non-target lesions.
4. Milairy lung metastases.
5. Gastric carcinoma not suited for exact measurement, because the tumor will not present exactly the same in a follow up scan due to position of the stomach and peristalsis.
6. Inguinal lymph nodes too small for target lesions (<15mm).

You do not measure non-target lesions, but make a good estimate.

In the follow up there are 3 possibilities:

- disappearance
- no disappearance (about the same)
- unequivocal progression (fig)



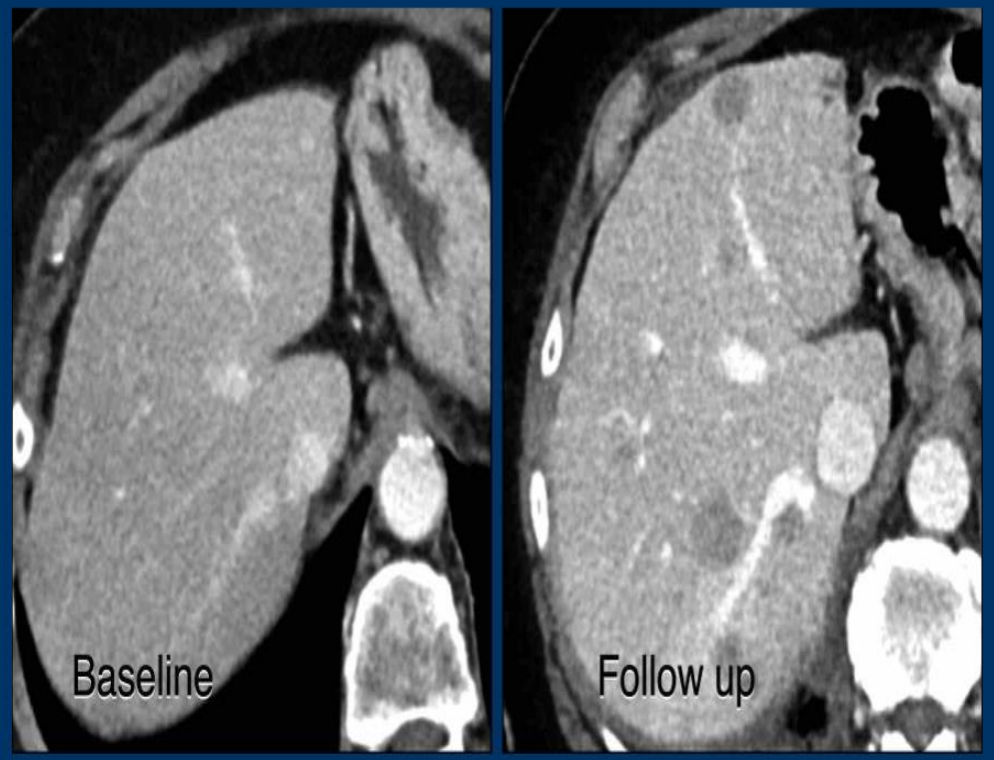
Here another example of progression of non-target lesions.

CT images in a 73-year-old male with progressive liver metastases of colorectal carcinoma.

At baseline the liver metastases were too small to be used as target lesions and consequently they were used as non-target lesions.
At follow up there is unequivocal progressions.

Unequivocal progression of non-target lesions means progressive disease, even if there is partial response or even disappearance of the target lesions.

New lesions



Any new lesion means progressive disease.

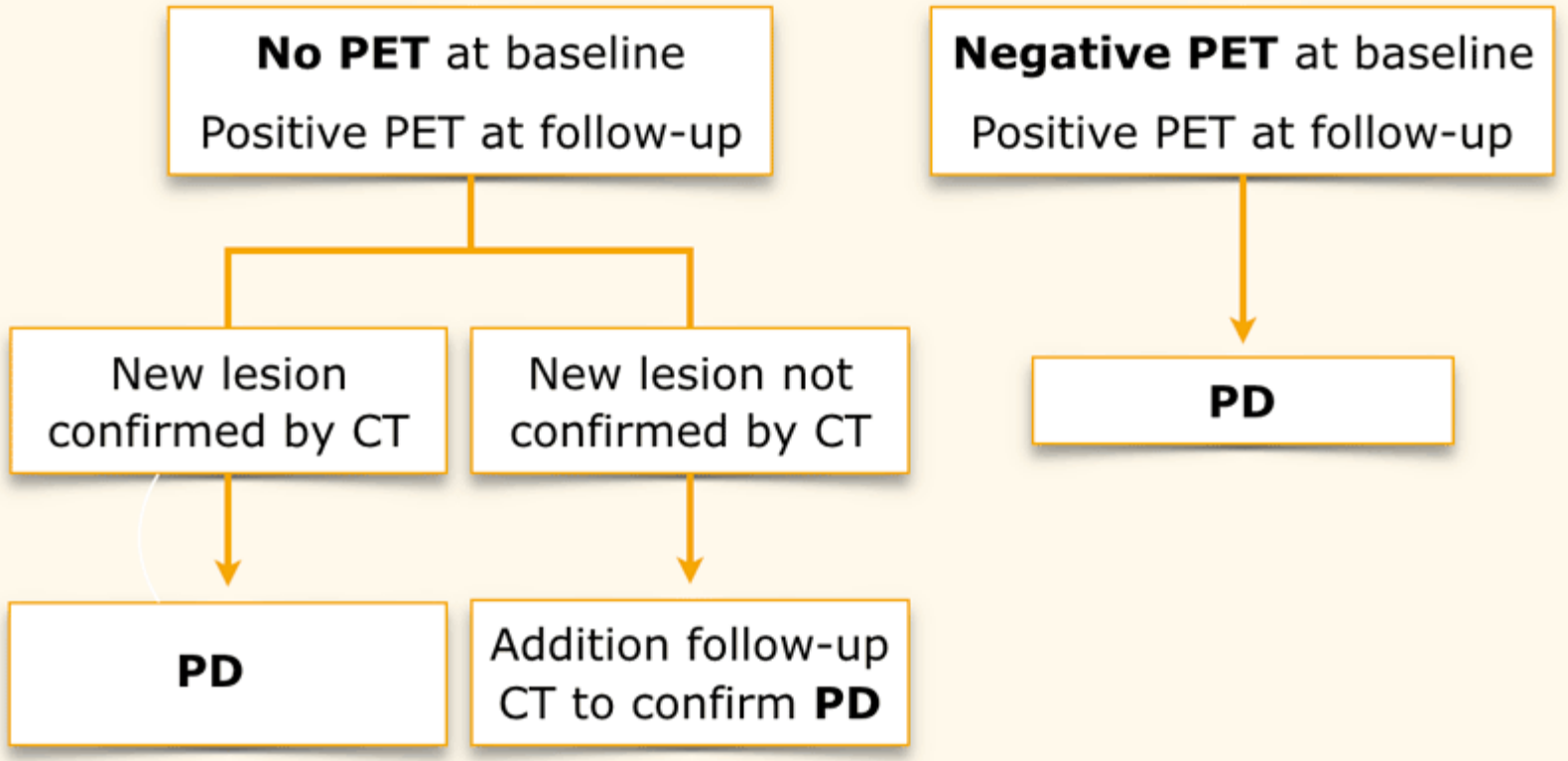
Do consider “new” lesions in an area of the body that was not imaged during baseline (for example brain metastases) as truly “new”, thereby forcing overall response to progressive disease.

CT-images in a 81-year-old female with endometrial carcinoma and occurrence of new liver metastases during treatment with chemotherapy.

Target lesions	Non-target lesions	New lesions	Overall response
CR	CR	No	Complete Response
CR	Non-CR / non-PD	No	Partial Response
PR	Non-CR / non-PD	No	Partial Response
SD	Non-CR / non-PD	No	Stable Disease
PD	Any	Yes / no	Progressive Disease
Any	PD	Yes / no	Progressive Disease
Any	Any	Yes	Progressive Disease

Response	Target lesions	Non-target	New lesions
CR	Disappearance of all target lesions	Disappearance of all non-target lesions	No
	Lymph node axis < 10 mm	Normalization of tumor marker levels	Partial Response
PR	30% ≥ decrease in SLD from baseline (≥ 4 weeks)	No progression	No
PD	≥ 20% increase in SLD from Nadir with an absolute SoD increase ≥ 5 mm	Unequivocally progression in lesion size	Yes, appearance of new unequivocally metastatic lesions
SD	Neither PR nor PD with the Nadir as reference point	Persistence of one or more non-target lesions and/or tumor markers > normal	No

FDG-PET in RECIST 1.1



		Baseline		1st assessment		2nd assessment		→ etc.	
		size (mm)	ima	size (mm)	ima	size (mm)	ima	size (mm)	ima
Target lesions	No. 1								
	No. 2								
	No. 3								
	No. 4								
	No. 5								
Sum of diameters									
% decrease in SLD* from **baseline**		NA							
% increase in SLD* from **nadir****		NA							
Non-target lesions		Presence		Presence or absence and extent		Presence or absence and extent		Presence or absence and extent	
New lesions		NA		Yes / no		Yes / no		Yes / no	
Other findings									
Radiologic response		NA		CR / PR / PD / SD		CR / PR / PD / SD		CR / PR / PD / SD	

Nodal staging

- **Nodal staging is crucial** because **tumor-positive lymph nodes are an independent predictor of poor survival for rhabdomyosarcoma**, influencing treatment stratification and radiation therapy.
- Regional nodal assessment should be performed according to RECIST 1.1.

1. Lymph nodes <10 mm are regarded as normal.
2. Lymph nodes 10-14mm are regarded as pathologic, but not suited for target lesions. They can be used as non-target lesions.
3. When target lymph nodes decrease to a normal size (<10 mm), their measurements still have to be included in the sum of the longest diamters (SLD).

- It is therefore recommended to consider as suspicious lymph nodes with FDG PET–positive criteria or **abnormal morphology at imaging**

Metastasis

- **The lungs and bone or bone marrow** are the primary sites of metastasis.
- **All patients should undergo noncontrast chest CT** and a **whole-body (head-to-toe) FDG PET/CT or PET/MRI at diagnosis to detect distant metastasis .**
- Also, most patients undergo neoadjuvant chemotherapy to allow complete tumor resection at surgery.

Rhabdomyosarcoma of Head and Neck

- Age
  - 70% < 12 years of age; 40% < 5 years of age

Location

- Up to 40% occur in head & neck

– **Parameningeal sites**: Middle ear, paranasal sinus, nasal cavity, nasopharynx, masticator space, pterygopalatine fossa, parapharyngeal space

□ Intracranial extension in up to 55%

□ Temporal bone involvement: Petrous apex & middle ear > mastoid

– **Orbit**

– **All other head & neck sites**: Scalp, cheek, parotid, oral cavity, larynx, oropharynx, hypopharynx, thyroid/parathyroid

Natural History & Prognosis

- Variable; depends on location & cell type
  - Orbit: Best prognosis (80-90% disease-free survival)
  - Parameningeal: Worst prognosis (40-50% disease-free survival)

  - Embryonal & pleomorphic: Better prognosis than alveolar RMS
  - Alveolar RMS without gene fusion: Prognosis is similar to embryonal RMS

Ultrasonographic Findings

- Solid, firm mass with variable internal vascularity
- May show bone destruction in superficial masses

CT Findings

- Invasive soft tissue mass with variable enhancement
- Osseous erosion is common but not seen in all cases

MR Findings

- Isointense T1, hyperintense T2 signal relative to muscle
  - Not "fluid bright" unless necrotic/cystic components

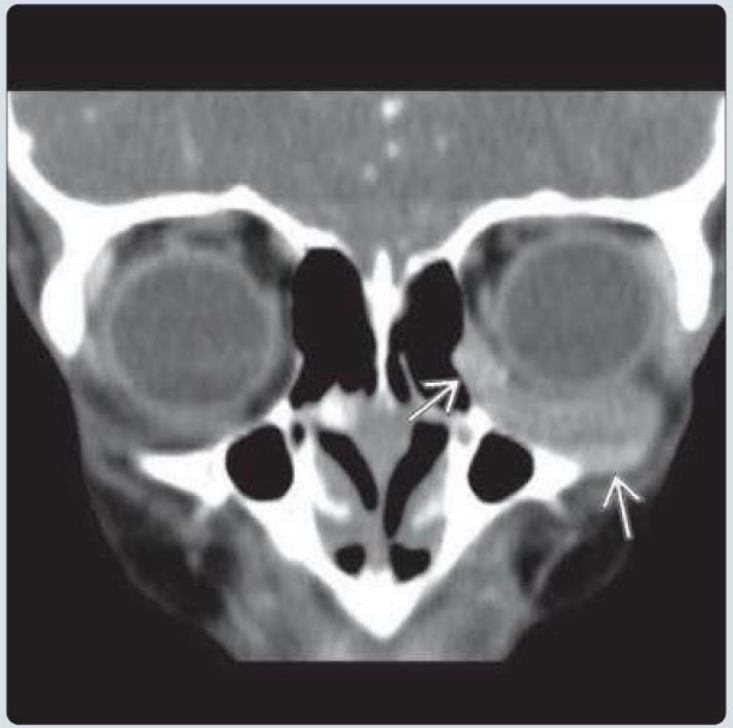
- Variable contrast enhancement, often mild to moderate
  - Diffuse, intense enhancement is atypical

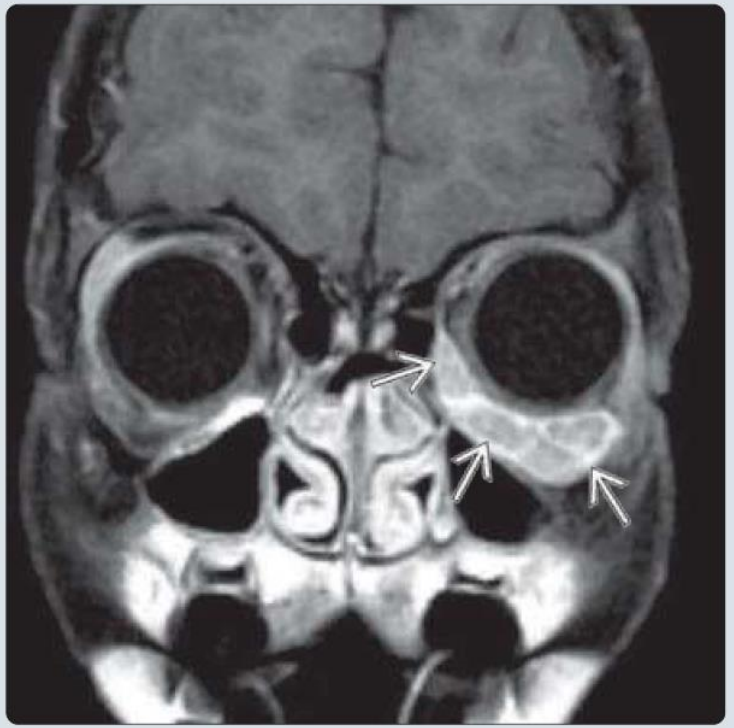
- Often restricts diffusion
  - ADC values range from ~ 0.5-1.3 x $10^{-3}/mm^2$

Nuclear Medicine Findings

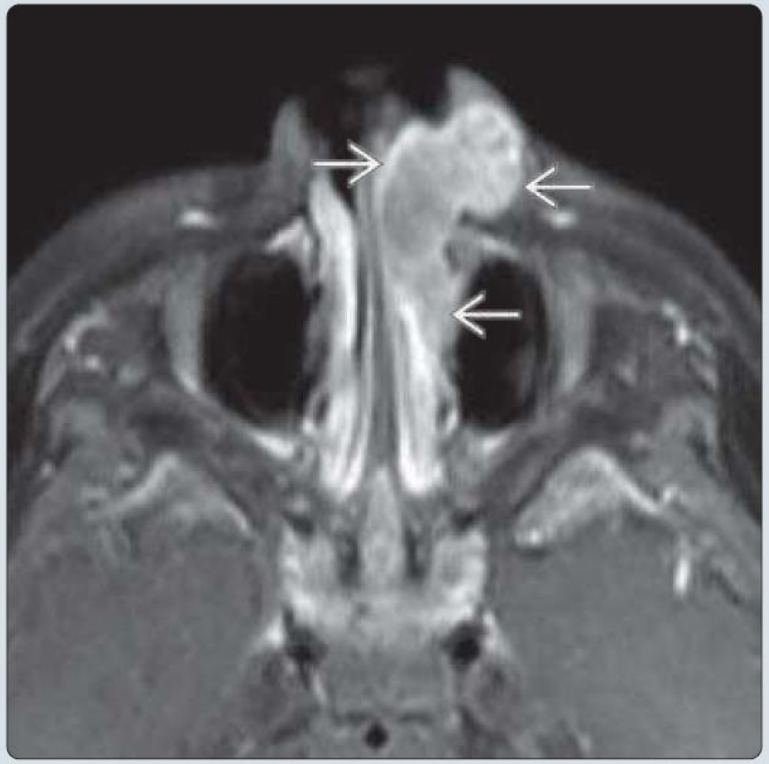
- PET/CT
  - Hypermetabolic
    - May improve staging & posttreatment evaluation

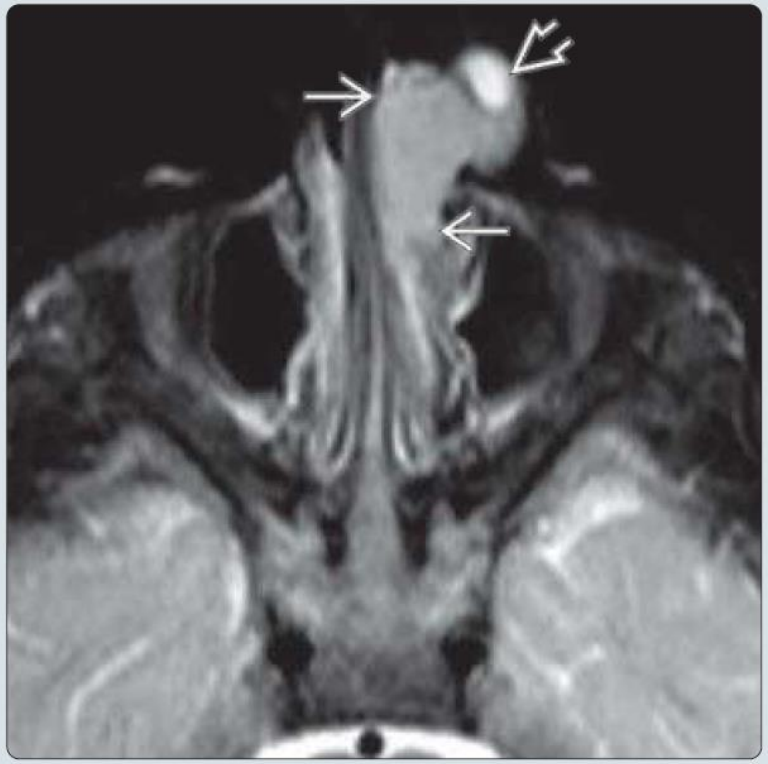
(Left) *Coronal CECT in an 8-year-old shows a nonspecific, mildly heterogeneous extraconal mass ➔ in the inferior & inferomedial left orbit without bone destruction.* **(Right)** *Coronal T1 C+ FS MR in the same child shows a heterogeneously enhancing mass ➔ with an atypical appearance for a hematoma, hemangioma, or vascular malformation. Biopsy confirmed an embryonal rhabdomyosarcoma. The absence of bone destruction does not exclude rhabdomyosarcoma (RMS).*

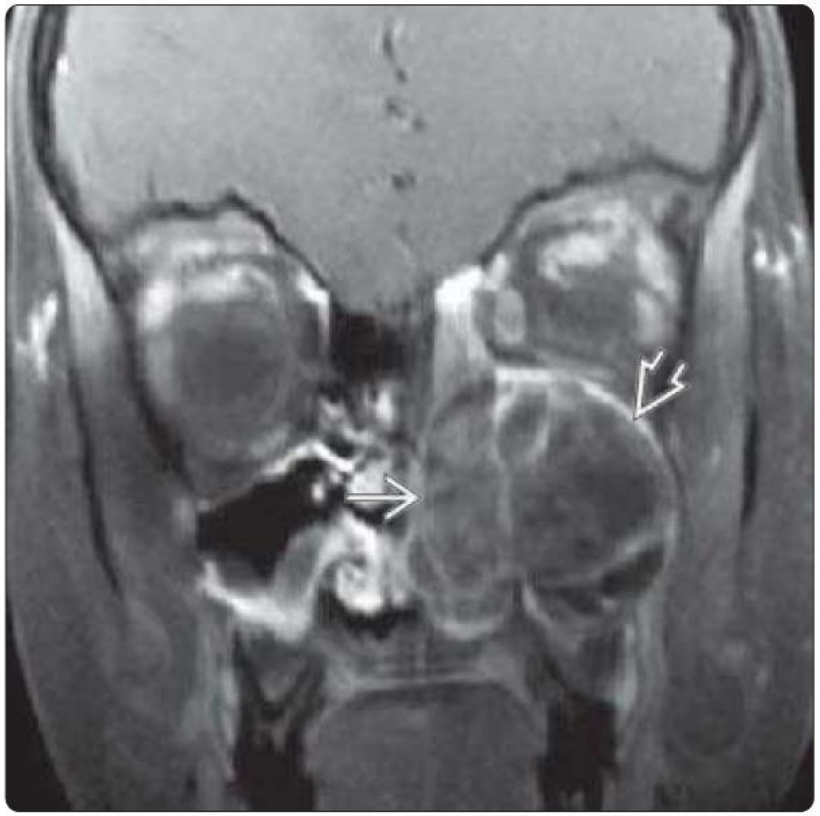


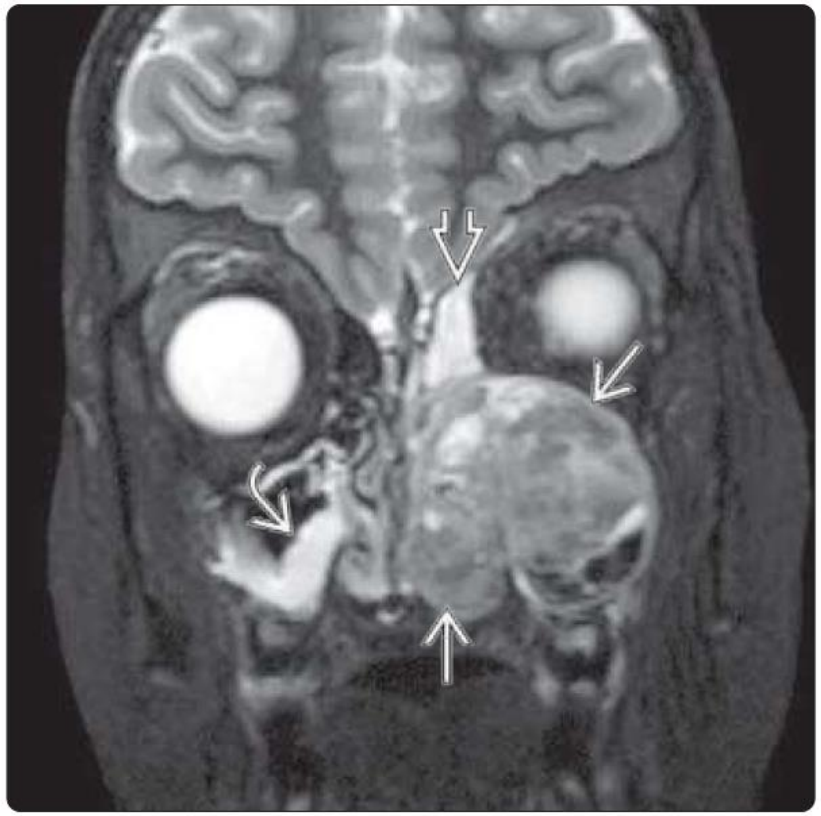


(Left) *Axial T1 C+ FS MR in a 15-month-old boy with intermittent epistaxis & swelling of the left nasal ala demonstrates a heterogeneously enhancing left intranasal/nasal alar mass ➡ obstructing the left nasal cavity.* **(Right)** *Axial STIR MR in the same patient demonstrates primarily intermediate signal intensity throughout the mass ➡ with the exception of a small cystic/necrotic region anteriorly ➡. Subsequent biopsy revealed an alveolar RMS.*

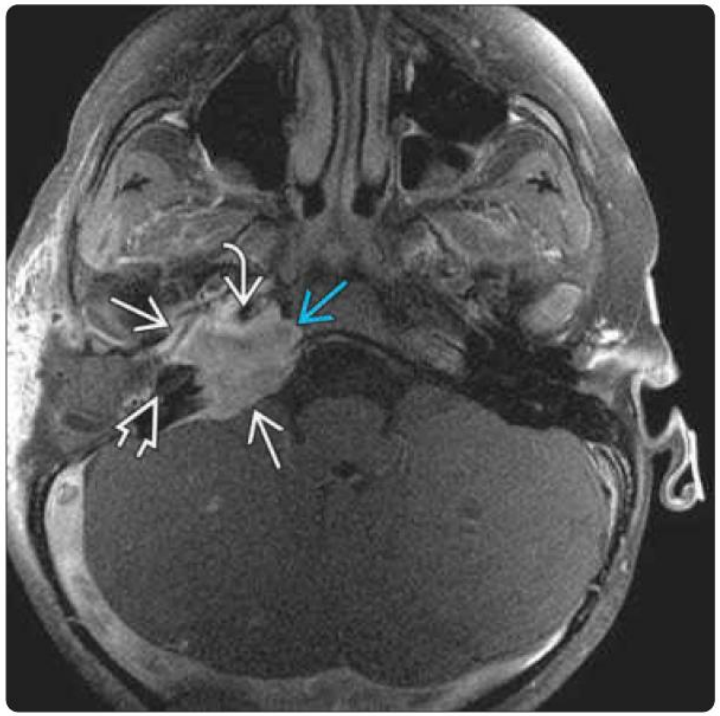


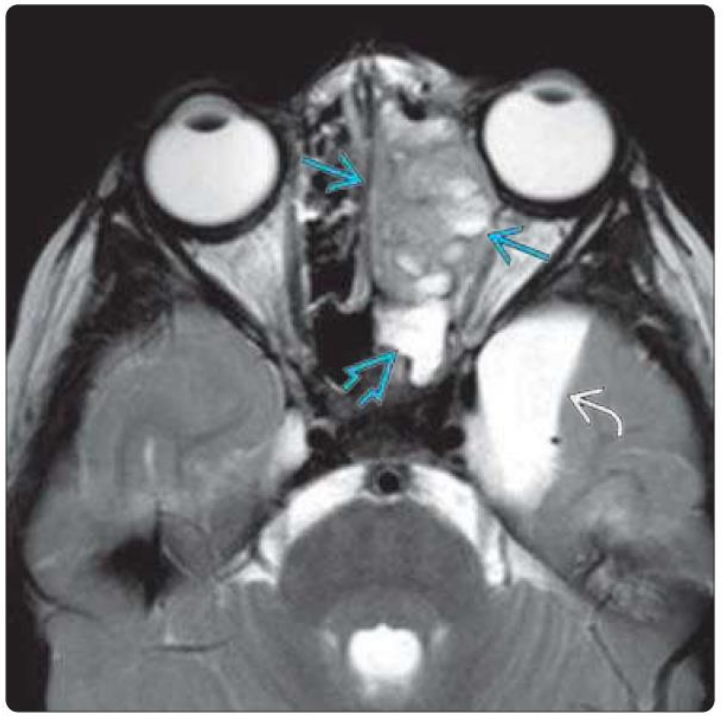






(Left) *Coronal T1 C+ FS MR shows a heterogeneously enhancing left nasal RMS ➔ with expansion of the left maxillary sinus ➔. Some component of the disease in the left maxillary sinus could represent inflammation rather than tumor.* **(Right)** *Coronal STIR MR in the same patient better differentiates the tumor ➔ filling the expanded left maxillary sinus & nasal cavity from hyperintense, inflammatory mucosal disease in the left ethmoid ➔ & right maxillary ➔ sinuses.*





(Left) *Axial T1 C+ FS MR demonstrates a moderately enhancing RMS ➔ destroying the right petrous apex & otic capsule bone adjacent to the cochlea ➔ & extending along margins of the internal carotid artery ➔ into the clivus ⇨.* **(Right)** *Axial T2 MR in a 5-year-old with left proptosis & palpable cervical adenopathy demonstrates a mixed-intensity alveolar RMS ⇨ as compared to the hyperintense sphenoid sinus inflammatory disease ⇨ & incidental middle cranial fossa arachnoid cyst ➔.*

Imaging Recommendations

- Best imaging tool
  - CT to evaluate osseous erosion
  - MR is best for soft tissue mass characterization
  - MR to evaluate perineural & intracranial spread of parameningeal RMS. Thickening & enhancement of nerves, leptomeninges
  - MR to distinguish between sinonasal tumor & obstructive/inflammatory disease

Protocol advice

- T2 FS or STIR MR: ↑ tumor conspicuity
- Coronal T1 C+ FS MR: Detect intracranial extension
- DWI MR: ADC values can help separate cellular tumor from benign vascular anomaly
- Axial & coronal thin-section bone CT: Osseous erosion
- Image neck: Rule out cervical metastatic adenopathy

Consider

- Not always associated with bone destruction
- Beware of enhancing soft tissue mass without bone destruction; may simulate infantile hemangioma (IH)
- IH is almost always found in 1st year of life; RMS is more common beyond 12 months
- IH is typically soft/compressible while RMS is more likely firm
- IH demonstrates high density of low-resistance arterial vessels on color Doppler
- IH enhances more intensely & homogeneously
- IH has higher ADC values on DWI MR

DIFFERENTIAL DIAGNOSIS

Infantile Hemangioma

- Benign vascular neoplasm in infants, often with characteristic cutaneous involvement
- Intensely enhancing round or lobulated mass with high-flow vessels during proliferative phase
- ASL MR shows markedly ↑ perfusion
- ADC MR values typically range from ~ 1.3-1.6 x 10^{-3}/mm²
- No bone destruction
- Fatty infiltration during involuting phase

Slow-Flow Vascular Malformation

- May be well defined or extensive/infiltrative
- Fluid signal contents ± layering blood products, retracted clots, or phleboliths (in venous type)
- Venous type shows gradual patchy enhancement; lymphatic macrocystic type shows thin septal enhancement
- ADC values typically range from ~ 2.0-2.6 x 10^{-3}/mm²
- ASL MR will not show ↑ perfusion

Fibromatosis Colli

- Benign, self-limited, heterogeneous mass within & expanding midportion of sternocleidomastoid muscle in young infant with torticollis

Metastatic Neuroblastoma

- Most cervical disease is due to metastatic adenopathy rather than primary lesion
- Metastatic disease to skull/skull base is frequently bilateral: Enhancing masses surround aggressive osseous permeation/expansion with radiating spicules of new bone

Langerhans Cell Histiocytosis

- Enhancing soft tissue mass filling sharply marginated punched-out lytic bone lesion
- Temporal bone: Mastoid > petrous apex & middle ear

Juvenile Angiofibroma

- Highly vascular mass causing nasal obstruction &/or epistaxis in adolescent males
- Intensely enhancing lesion with bone destruction & internal high-flow vessels
- Originates at sphenopalatine foramen on lateral nasal wall
- Often involves nasal cavity, nasopharynx, skull base, masticator space ± orbit, sinus, intracranial extension

Nasopharyngeal Carcinoma

- Nasopharyngeal mass in 2nd decade of life
- Variable contrast enhancement
- Central skull base erosion, widening of petroclival fissure, extension to pterygopalatine fossa + masticator & parapharyngeal spaces
- Unilateral or bilateral cervical & lateral retropharyngeal adenopathy

Non-Hodgkin Lymphoma

- Non-Hodgkin lymphoma & Hodgkin lymphoma imaging findings are similar; difficult to differentiate
- Large, nonnecrotic nodes are typical
- Sinonasal, orbital, or nasopharyngeal NHL may cause osseous erosion

Plexiform Neurofibroma

- Benign peripheral nerve sheath tumor in neurofibromatosis type 1
- Lobulated masses with peripherally ↑ T2 signal & centrally ↓ T2 signal (target sign)
- Bone remodeling, typically without destruction

2. Stage Grouping (IRS / TNM-Based)

Stage	Criteria
Stage I	Favorable sites (orbit, head/neck non-parameningeal, genitourinary **excluding bladder & prostate**), any T and N, M0
Stage II	Unfavorable sites such as bladder, prostate, extremities, parameningeal; T1a or T2a (≤5 cm), N0 or Nx, M0
Stage III	Unfavorable sites with either: T ≤5 cm and N1, or T >5 cm (T1b/T2b), N0/N1, M0
Stage IV	Any site, any T/N, with distant metastasis (M1)

> **Note:** Favorable sites = orbit, head/neck non-parameningeal, genitourinary **except bladder & prostate**. Bladder and prostate are considered **unfavorable**.

✅ Indications for Image-Guided Biopsy

- **Deep-seated tumors**:
  - Parameningeal head & neck (nasopharynx, paranasal sinuses, skull base).
  - Infratemporal fossa / parapharyngeal space.
  - Orbital apex lesions.
  - Retroperitoneal or pelvic RMS.
  - Prostate, bladder, vaginal, or paratesticular tumors not accessible safely by open approach.
- **When open/excisional biopsy would be mutilating or high-morbidity** (e.g., orbital exenteration, trans-oral/pharyngeal dissection).
- **When tumor is unresectable at presentation** and tissue is only needed for diagnosis, not excision.
- **Need for precise localization** to avoid damage to critical structures (optic nerve, carotid, urethra, bladder neck).
- **Minimally invasive approach preferred** in small children to reduce morbidity, hospital stay, and complications.

❌ Contraindications for Image-Guided Biopsy

Absolute

- **Uncorrectable coagulopathy** (risk of severe bleeding).
- **Unstable patient** who cannot tolerate sedation/anaesthesia.
- **Infection at biopsy site** (risk of seeding deeper tissues).

Relative / Situational

- **Superficial, easily accessible mass** → open/incisional biopsy may be preferred (e.g., paratesticular or easily palpable neck mass).
- **Very small lesion (<1–2 cm)** where needle biopsy may yield inadequate tissue.
- **Need for extensive sampling** (e.g., if lymphoma vs RMS is suspected and large tissue is required for flow cytometry + molecular studies).
- **Lesion abutting vital structures** where safe needle trajectory cannot be established (e.g., cavernous sinus, brainstem, vascular encasement).
- **Previous biopsy scar tract planning** — if biopsy tract would contaminate uninvolved compartments or make future resection difficult, alternative route may be chosen.

Rhabdomyosarcoma, Musculoskeletal

- Extremities (15-20%)

– Typically intramuscular

- Truncal/retroperitoneal (11-17%)

- Embryonal: < 15 years old; head & neck, GU

□ 46% occur in patients < 5 years old

- – Alveolar: Typically adolescents & young adults (extremity, paratesticular, & truncal)

□ Occurs at all ages

- Morphology

○ Usually round with well-circumscribed, lobular margins

○ May have tail of tumor extending proximal/distal

Imaging findings

- **Radiographic Findings**

• Soft tissue fullness similar to muscle density on radiographs

• Rarely shows adjacent bone involvement

• Ca^{2+} is not typical

- **CT Findings**

• Not used for primary mass investigation

• Lung CT for metastatic work-up

- **Ultrasonographic Findings**

• Solid, firm, mildly heterogeneous soft tissue mass with variable amounts of internal vascularity

• Often round & well-circumscribed, though deeper infiltration is possible

Imaging findings

MR Findings

- T1WI
  - Similar signal to skeletal muscle
- T2 FS/STIR
  - Moderately to markedly hyperintense to skeletal muscle
  - – Not typically cystic
  - Can be heterogeneous with necrosis & hemorrhage
  - Typically minimal (if any) surrounding edema
- T1WI C+ FS
  - Variable enhancement, ranging from minimal to diffuse,
  - heterogeneous to homogeneous
- DWI
  - Typically restricts diffusion; can ↑ conspicuity of primary & metastatic lesions
  - – Mean ADC values reported from 0.7-1.2 x 10^{-3} mm/s^2
- MRA/MRV
  - ○ May be helpful to determine relationship of mass to neurovascular bundle

Nuclear Medicine Findings

- PET
  - Intense FDG uptake by soft tissue tumor
  - Better than conventional imaging in staging disease (except for very small lung lesions)
  - May not predict event-free survival in intermediate- or high-risk RMS

Imaging Recommendations

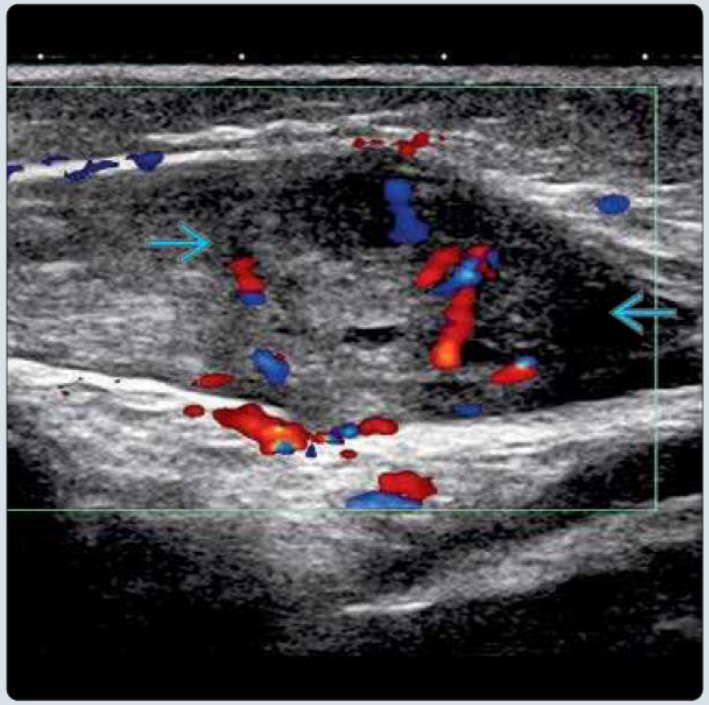
- Best imaging tool
- US & MR features can strongly suggests sarcoma
- MR is better at defining deep extent & relationship to critical structures (e.g., neurovascular bundle, joints, etc.)
- Extremity RMS: Important to image entire extremity, including lymph node drainage basins

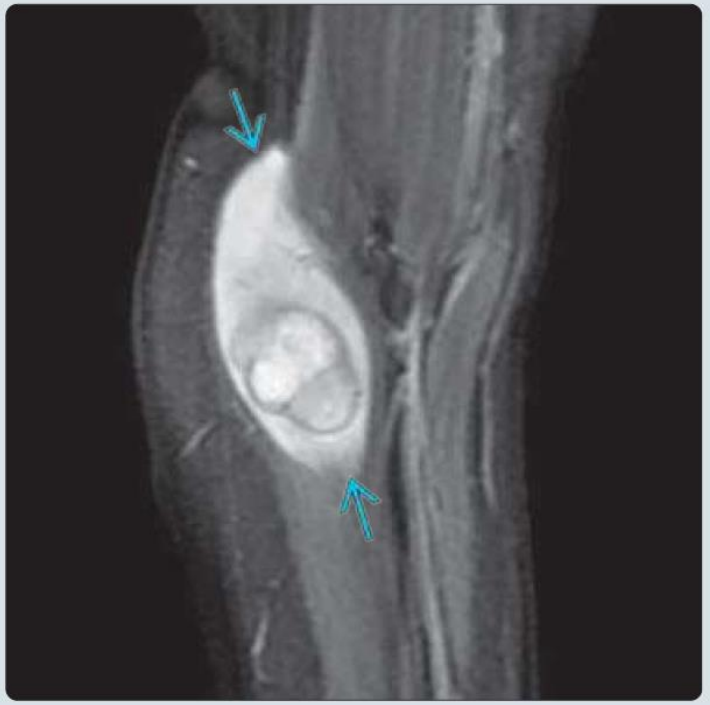
Protocol advice

- Consider subtraction MR images of pre- from postcontrast T1 FS

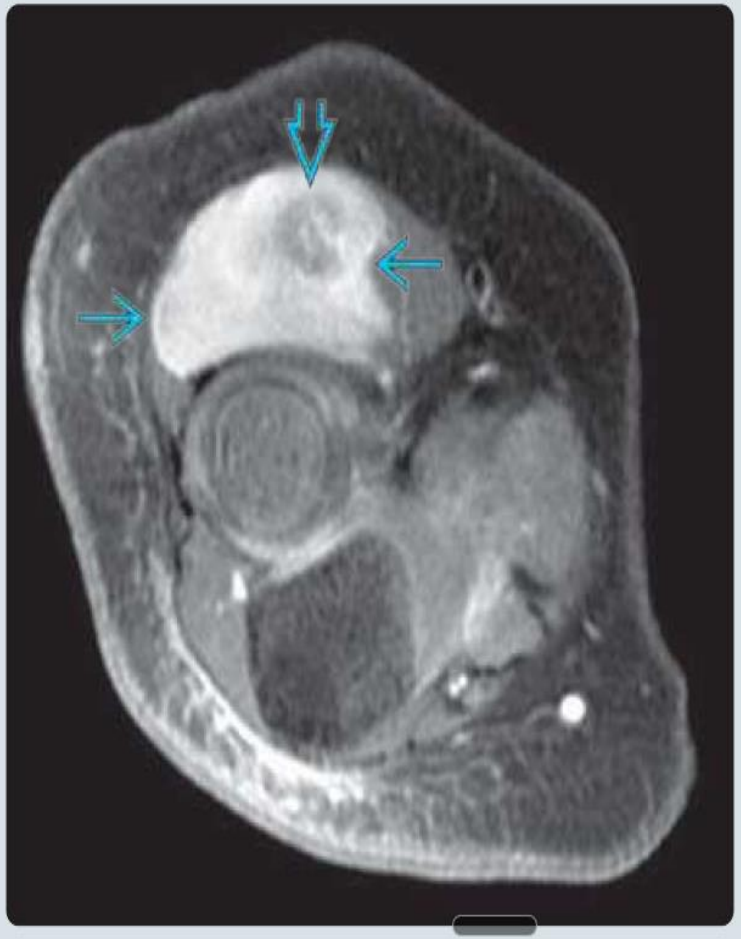
– Avoids pseudoenhancement postcontrast due to preexisting hemorrhage, protein, etc

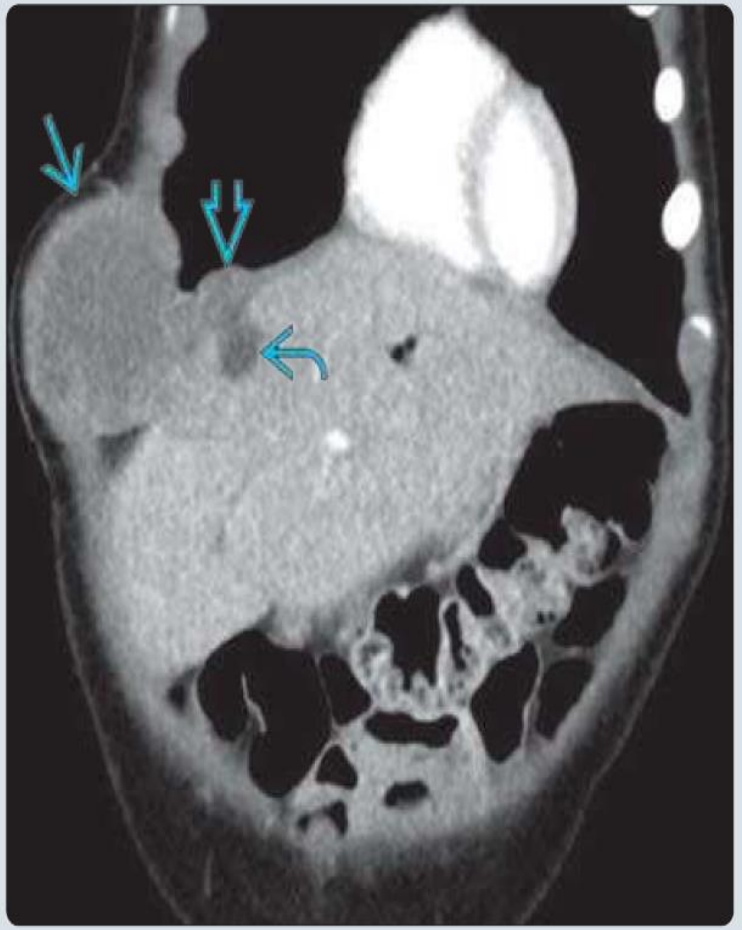
(Left) *Longitudinal color Doppler US in a 12-month-old with weeks of arm swelling shows a heterogeneous, ovoid, intramuscular soft tissue mass ⇨ with moderate internal vascularity. The mass showed no significant deformation upon compression by the transducer.* **(Right)** *Coronal STIR MR in the same infant shows mild internal heterogeneity of the predominantly hyperintense mass ⇨, which involved the brachioradialis & extensor carpi radialis muscles.*





(Left) *Axial T1 C+ FS MR in the same infant shows nearly uniform enhancement of the forearm rhabdomyosarcoma (RMS) with a central region of necrosis &/or hemorrhage. Diffusion restriction (not shown) was variable in the mass with ADC values ranging from 0.8-1.2 x 10^{-3} mm/s².*
(Right) *Coronal CECT in a 21-month-old with an enlarging chest wall mass shows deep extension of the predominantly superficial mass into the diaphragm & liver. RMS was proven at biopsy.*





📋 Image-Guided Biopsy of Soft Tissue Rhabdomyosarcoma

Indications	Contraindications
Suspicious soft tissue mass requiring histological confirmation	**Absolute:**
Subtyping & molecular studies (IHC, cytogenetics, PAX-FOXO1 testing)	– Uncorrectable coagulopathy (INR >1.5, platelets <50k)
Unresectable or borderline resectable lesion (before chemo/radiotherapy)	– Hemodynamic instability
Suspected recurrence (differentiate relapse vs fibrosis/necrosis)	– Patient uncooperative with no safe sedation option
Biopsy of suspected metastatic site	**Relative:**
When open biopsy is high risk (deep retroperitoneal, pelvic, mediastinal, paraspinal)	– Lesion inaccessible without injuring vital structures
	– Vascular lesion suspected (risk of hemorrhage)
	– Local infection at puncture site
	– Small, easily resectable lesion (excisional biopsy preferable)
	– Biopsy tract contamination risk (must plan incision with surgical team for later excision)

DIFFERENTIAL DIAGNOSIS

Other Soft Tissue Sarcomas

- Synovial sarcoma
  - Ca^{2+} in 1/3, may be small & cystic-appearing
  - Usually not intraarticular but near joint; often abuts bone
- Extraosseous Ewing sarcoma
  - Similar in appearance to RMS, usually 2nd-3rd decades
- Fibrosarcoma
  - Typically infantile in children
  - May be highly cystic or solid & highly vascular
  - Frequently infiltrative

Plexiform Neurofibroma

- Most common in neurofibromatosis type 1 (NF1)
- Lobular masses following course of nerve
- Classic target appearance in cross section on T2/STIR MR
  - Bright periphery, intermediate/dark center
- Loss of target appearance & disproportionate growth suggest malignant degeneration

Venous Malformation

- Patchy enhancement, fluid-fluid levels, ± phleboliths

Infantile Hemangioma

- Solid but soft subcutaneous mass of infants with mild lobulations, variable echogenicity
- Highly vascular on color Doppler US with > 5 vessels/cm^2
  - Low-resistance arterial waveforms during proliferation

Myositis Ossificans

- Heterogeneous intramuscular mass in older children with prior acute trauma (2/3) or microtrauma history
- Marked inflammatory reaction of surrounding muscle
- Calcifies peripheral to central over weeks/months

Abscess

- Heterogeneous collection with thick, irregular wall & septations; swirling internal debris with compression
- Peripheral hyperemia/enhancement
- Moderate to marked surrounding edema

Nonrhabdomyosarcoma soft tissue sarcomas (NRSTS)

Definitions

- Soft tissue sarcomas: Heterogenous group of malignancies arising in extraskeletal mesenchymal tissues
- In children: ~ 40% are rhabdomyosarcoma, ~ 60% are NRSTS
- > 40 subtypes of NRSTS (e.g., synovial sarcoma, infantile fibrosarcoma, malignant peripheral nerve sheath tumor, undifferentiated sarcoma, extraskeletal Ewing sarcoma, etc.)

Role of Imaging

- As in all soft tissue tumors, radiologic imaging plays an important role in NRSTS in suggesting the diagnosis, staging, targeting or guiding biopsy, and planning and monitoring local control.
- Quantitative imaging techniques may help to further characterize tumor tissue by providing parameters related to the tumor microenvironment.
- Lung and whole-body imaging are needed to detect metastases.
- However, given the rarity and inhomogeneity of histological subtypes, there is little literature evidence for the optimal imaging approach in NRSTS.

Summary of recommendations.

	STAGING (within 28 days)	DURING TREATMENT	OFF THERAPY SURVEILLANCE
Primary tumor with MRI[a]	•	•	•
Locoregional lymph nodes[b]	•		
Pulmonary metastases, chest CT/chest x-ray[c]	•	•	•
Distant lymph nodes and extra-pulmonary metastases, ^{18}F-FDG-PET CT /MRI[d]	•	•	•
Whole body MRI[e]	•	•	•
Brain MRI[f]	•		

Primary tumor with MRI

- Use same mode of investigation of tumor sites throughout the treatment and during follow-up. Frequency according to treatment protocol, at least before local treatment and at completion of induction treatment (approximately every 3–4 months). During off-therapy surveillance, we recommend imaging of the primary site every 3–4 months, with the same modality and technical settings used at baseline for the first two years off therapy. Thereafter individual characteristics should be considered.

Biopsy

- After appropriate imaging assessment, the standard approach to diagnosis of an NRSTS, as with RMS, consists of multiple image-guided (ultrasound whenever possible) core needle biopsies, preferably with a 16 gauge or larger needle.
- The biopsy should be carried out at large referral centers by experienced interventional radiologists or surgeons after multidisciplinary discussion. The interventional radiologist should be aware that the biopsy tract and subsequent scar must be resected during definitive surgery because of the potential for tumor cell seeding

Assessment of locoregional lymph node involvement

- In general, involvement of locoregional lymph nodes is rare in NRSTS, with rates of 3–4% . Therefore, locoregional lymph node assessment is not required for most histotypes.
- Assessment of locoregional lymph nodes is suggested for patients with epithelioid sarcoma, angiosarcoma, alveolar soft part sarcoma (ASPS), and clear-cell sarcomas (CCS)
- In addition, locoregional lymph node assessment is suggested for children with an extracranial malignant rhabdoid tumor, because of its tendency for nodal metastasis
- Timing of locoregional lymph node assessment will be decided by treating physicians: some centers include locoregional lymph nodes in the primary tumor assessment, others perform additional imaging once the histologic diagnosis is confirmed

Assessment of locoregional lymph node involvement

- There is no evidence available to advocate for a specific technique for evaluation of lymph node involvement in NRSTS. Most commonly, locoregional lymph nodes will be assessed with MRI during primary tumor evaluation. However, for superficial lymph nodes, ultrasound could be used, provided there is sufficient expertize for the acquisition and interpretation of images
- In contrast to RMS, there is no literature regarding the prognostic value of sentinel lymph node diagnostics; prospective studies are needed to determine the value of sentinel lymph node diagnostics in NRSTS patients at increased risk of lymph node involvement.

Assessment of locoregional lymph node involvement

- Lastly, malignant lymph nodes can be FDG avid on 18FFDG- PET CT but other explanations for FDG avidity, such as infection or recent vaccination, must be considered during interpretation.
- If there is uncertainty or inconsistent findings, lymph node, core needle biopsy or excision is recommended for pathologic evaluation. Fine needle aspiration (FNA) is discouraged because of the risk of sampling error leading to subsequent false negative findings and the risk of seeding along the biopsy tract.

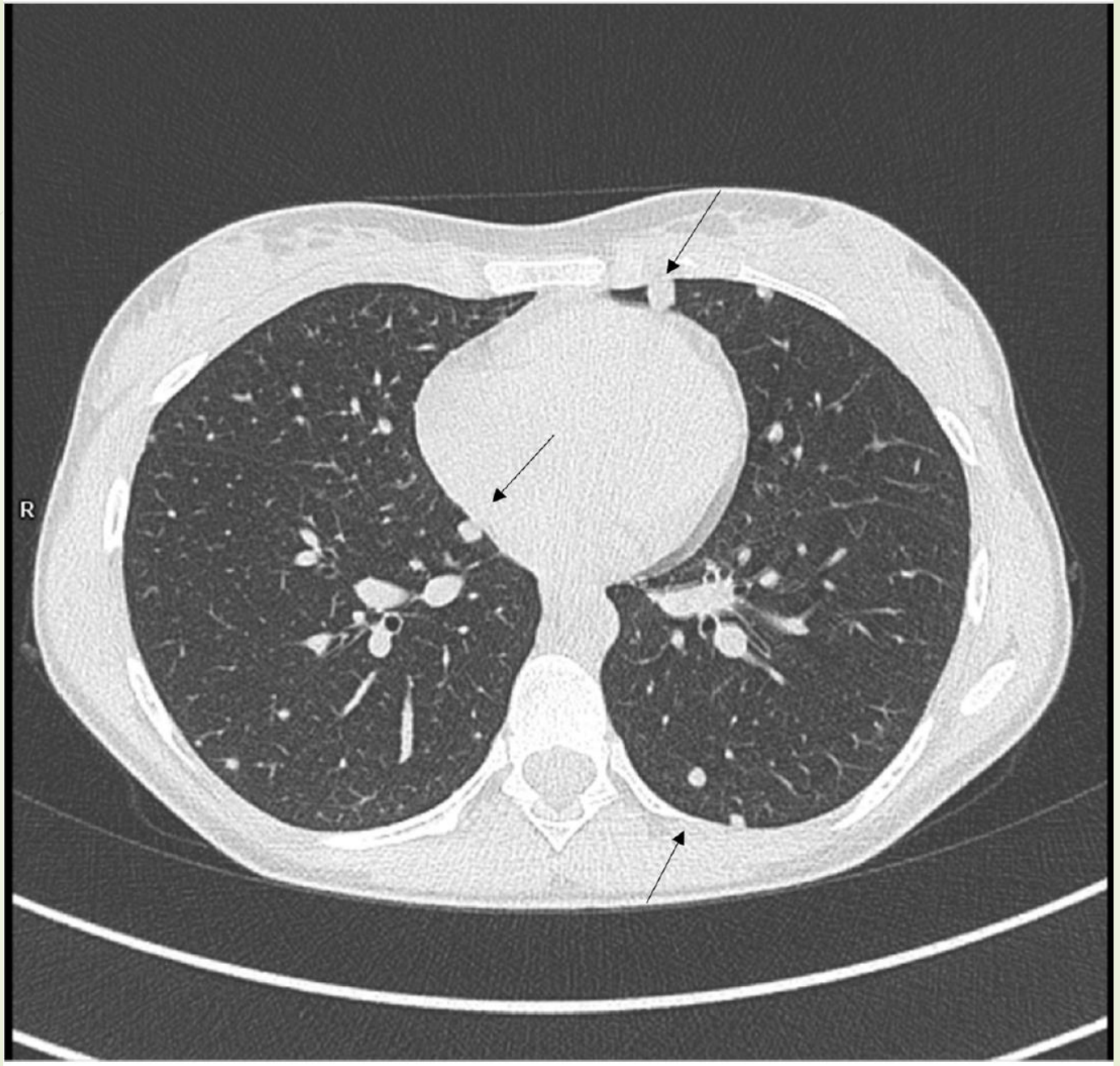
Assessment of distant metastases

- The risk of metastatic disease in patients with NRSTS is generally low. The prevalence of metastatic disease in the more aggressive subtypes of adult-type NRSTS and synovial sarcoma has been reported as 5–15%

- In more than 60% of metastatic cases, the metastases are confined to the lungs. The risk of extra-pulmonary metastases is even lower and usually occurs concurrently with lung metastases

Lung metastases

- The lung is the most common site for metastases in NRSTS patients but the risk for spread to the lungs depends on the histology, the size of the primary tumor, and its biologic behavior . We recommend assessment for lung lesions in all NRSTS. Chest CT is the most commonly used technique for the evaluation of lung metastases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Lung metastases

- However, because lung metastases very rarely occur in low risk NRSTS (i.e. FNCLCC grade 1 or 2, small tumor size (< 5 cm), and/or completely resected at diagnosis (IRS I)), workup by chest CT could be replaced by chest x-ray (XR, in two orthogonal planes). Workup with chest x-ray is not common practice in most pediatric oncology centers, but with the increasing costs of patient care, we advocate for critical reconsideration of current practice and reduction of using repeated ionizing radiation in patients with low risk of metastatic or recurrent disease.

Lung metastases

- Historically, lung nodules are considered metastatic, in European treatment protocols, if they meet one of the following criteria;
- 1) there is ≥ 1 pulmonary nodule measuring ≥ 10 mm
- 2) two or more welldefined nodules measuring ≥ 5 mm but< 10 mm or
- 3) ≥ 5 welldefined nodules measuring< 5 mm.

- Pulmonary lesions not fulfilling one of these criteria can be considered as indeterminate for malignancy

Lung metastases

- Healthy children are known to have pulmonary nodules that may be inflammatory or infectious in nature and investigators have found that there is no size cut-point that can reliably distinguish benign from malignant nodules in children . In some geographic areas, certain infections such as histoplasmosis and mycobacterium tuberculosis, are endemic and these should be considered in the differential diagnosis when evaluating pulmonary nodules. In these cases, a biopsy can be considered for confirmation.

- Percutaneous needle biopsies, however, are subject to sampling error and could result in a false negative report.

Lung metastases

- Furthermore, the prognostic relevance of small lung nodules is uncertain.
- Importantly, those soft tissue sarcomas that spread to lymph nodes (e.g. RMS) are known to behave as a systemic disease, with the potential for microscopic metastases at diagnosis.

Extra-pulmonary metastatic sites

- Extra-pulmonary metastases are rare in children with NRSTS and even rarer in patients with NRSTS that have no lung metastases
- Nevertheless, it is currently accepted in pediatric sarcoma diagnostics that if the primary tumor is FDG avid, 18F-FDG-PET CT can be used for the detection of distant lymph node and soft tissue metastases.
- We recommend 18F-FDGPET CT in all NRSTS patients with lung metastases (any grade) for the detection of extra-pulmonary disease.

Extra-pulmonary metastatic sites

- For patients with FNCLCC (Federation Nationale des Centres de Lutte Contre Le Cancer) grade 3 NRSTS (including without lung metastases) staging with 18F-FDG-PETCT could be considered by the multidisciplinary team. Ideally, this
- imaging data should be collected within a trial so more can be learned about the prognostic value of 18F-FDG-PET CT in NRSTS

- In contrast to other NRSTS, myxoid liposarcomas (MLS) can present with extra-pulmonary disease in the absence of lung metastases. Further, these patients can develop metastases or a synchronous primary, in unusual sites such as the spine or soft tissue . These metastatic lesions can occur up to eight years after initial diagnosis. MLS often have minimal FDG avidity and, therefore, whole body MRI (WB-MRI) is recommended for follow-up of these patients

Extra-pulmonary metastatic sites

- **Because alveolar soft part sarcoma, clear-cell sarcoma and angiosarcoma have a propensity to metastasize to the brain, brain MRI is recommended in the staging evaluation of these patients**

Response assessment

- In measuring NRSTS treatment response by cross-sectional imaging, either one-dimensional (1D) or three-dimensional (3D) methodology has been used .
- The prognostic value of tumor size response has been debated in RMS, based on several studies with conflicting results .
- Fewer studies have been conducted in NRSTS but suggest that patients with at least minor partial response (minor PR, i.e.>33% volume reduction) have better outcome than those who have stable (SD) or progressive disease (PD) (i.e.<33% decrease or an increase in volume, respectively)

Response assessment

- Based on available evidence, no definitive recommendations can be made for 1D or 3D measurements at present and individual protocol recommendations should be followed. The response evaluation criteria in solid tumors (RECIST, version 1.1) are more commonly used in adult sarcoma practice and early phase clinical trials and have the advantage of providing clear measurement guidelines.

Response assessment

- NRSTS can be an elongated spindle shaped mass and hypothetically 3D assessments would give a more accurate estimation of the actual tumor size. Until now, no evidence has been provided to support this hypothesis and a study comparing 1D and 3D measurements in an RMS population revealed that neither method was superior, with significant interobserver variability for both techniques

Response assessment

- Regardless of the method used, data should be interchangeable and, therefore, the same size cutoffs should be used to qualify for disease progression as well as response. Historically, PD was defined as a 25% increase in the sum of products of maximal perpendicular diameters (2D, WHO criteria) or 40% increase in volume (3D, E*p*SSG and COG criteria), which is comparable to only a 12% increase in 1D (RECIST). To avoid classifying patients as having progressive disease too easily, the cutoff for PD was increased to 20% in 1D with the introduction of RECIST 1.0 ,This equals to 73% increase in volume and is recommended as a cutoff for NRSTS (and RMS) response assessment

Response assessment

- With the introduction of new treatments with targeted molecules or immunotherapeutics, the discussion on response assessment has become more complicated . It is well known that immunotherapy (e.g. checkpoint inhibitors) may initially reveal pseudoprogression before actual tumor size reduction or result in hyperprogression, a dissociated response, or a durable response

- Additionally, change in contrast enhancement using dynamic MRI and degree of diffusion restriction may be more reliable prognosticators than change in size, especially in entities such as synovial sarcoma that tend to show moderate change in size under therapy

Response assessment

- More recently, the nuclear medicine community published a practice guideline with recommendations for the use of 18F FDG PET-CT during immunomodulatory treatments in patients with solid tumors . One of the points raised by the authors, is the potential occurrence of immune-related adverse events, which can occur in any organ and are hypermetabolic on 18F-FDG PET-CT. These immune- related adverse events should not be mistaken for disease progression. Further international or multicenter studies are needed to investigate the prognostic value of 18F-FDG PET-CT, (semi-) quantitative MR imaging, the best PD criteria, and the development of alternative imaging techniques to predict response in pediatric NRSTS.

Imaging during treatment

- In pediatric sarcoma protocols, imaging is usually performed at staging, after three to four courses, and at the end of treatment.
- Evaluation of the primary tumor and locoregional lymph node stations should ideally be done with the same imaging modality and machine parameter settings used at diagnosis.
- Large field MRI should be used to cover both the primary tumor and locoregional nodal drainage site.
- Pulmonary nodules should be monitored with chest CT.

- In patients with localized disease and a low grade primary tumor (i.e. FNCLCC grade 1 or 2), a follow-up chest CT is proposed to be replaced by chest x-ray

Imaging during treatment

- During treatment, the disappearance or occurrence of any non-pulmonary metastases should be monitored.
- There is insufficient evidence on the prognostic value of 18FFDG PET CT or WB-MRI response in these patients, but these techniques are most used to evaluate metastatic lesions

Imaging during treatment

- For the interpretation, it should be mentioned that equivocal 18F-FDG-PET CT lesions should be confirmed with biopsy.
- Notably, bone signal abnormalities can persist for a prolonged period on MRI even though adequately treated.

Off therapy surveillance

- Surveillance after treatment completion aims to detect recurrence of disease as early as possible, hoping to improve outcome by initiating treatment while disease burden is still low
- In a recently published retrospective study of children with NRSTS who relapsed following upfront localized disease, outcomes were poor with a 5-year OS of 26%, and was depending on the type and timing of the relapse (local and late relapses have better outcome) and if a secondary remission could be achieved

- While the lung was the most common metastatic site at relapse, the recurrences were somewhat evenly distributed between local, metastatic and a combination.

Off therapy surveillance

- In the same series, the investigators are analysing the potential value of off-therapy regular follow-up by comparing the outcome of patients in whom relapse was detected by routine imaging and patients in whom relapse was first suspected by symptoms .
- The authors showed that time to relapse was similar in the two groups
- While the value of routine scanning of primary site seemed limited (routine imaging was able to detect a small proportion of local relapses), the study showed that surveillance identified 31/48 distant relapse (in particular 79% of lung metastases).

- Overall survival (OS) at 5 year was 34% for the symptoms group, and 24% for the imaging group; however, in patients with lung metastatic relapse, 5- year OS was statistically better for the imaging group, i.e. 25.8% versus 0% for the symptoms group.
- This suggested that radiological surveillance may have a value in the detection of lung relapse, and in increasing survival for this patient category

Off therapy surveillance

- Two adult STS studies evaluated the utility of surveillance imaging in select patient populations with extremity primaries. Rothermundt et al. reported that local relapse was almost always detected by patients/providers due to signs or symptoms, thus suggesting that imaging of the primary site is of doubtful benefit
- The same investigators reported that routine chest x-ray may be useful to detect lung metastases that are suitable for surgical resection
- Cheney et al. focused on local relapse and reported that surveillance imaging detected an asymptomatic local relapse in 2 out of 114 cases . They concluded that surveillance imaging should be limited to patients whose primary tumor sites are not easily assessed by physical examination.

Off therapy surveillance

- In summary, the issue of whether off therapy surveillance imaging may lead to an earlier detection of tumor recurrence and subsequent improved survival is unknown.
- Within that context, it is important to consider the potential negative effects of using excessive surveillance radiological exams in cancer survivors including anxiety and distress around the imaging findings
- cost, and late effects with prolonged exposure to ionizing radiation in an already vulnerable population

Off therapy surveillance

- the absence of extensive evidence-based data in children, incorporating identified variables of relapse (histologic subtype, timing after therapy), the RMS experience, and published studies in patents with NRSTS should guide decision making on the use of imaging and the frequency in pediatric NRSTS.

Off therapy surveillance

- For patients treated for localized NRSTS we suggest imaging of the primary site with MRI and of the lungs with chest XR every three to four months for at least the first two years after treatment completion.

- CT chest is recommended for better characterization when suspicious lesions are found on chest x-ray.
- For patients initially treated for metastatic NRSTS chest x-ray could be replaced by chest CT, but discussion with the family is recommended: there is no evidence supporting chest x-ray or chest CT in this population and outcome after relapse in these patients, in general, is very poor.

Off therapy surveillance

- After two years, individual characteristics should be considered when deciding to continue or discontinue further follow up with imaging of the primary tumor site. In patients with extremity primaries, physical examination with or without ultrasound may suffice
- Longer follow-up (up to 5 years) could be considered for the evaluation of pulmonary metastases with chest x-ray: every six months in the third year and once yearly in the fourth and fifth year.
- Follow-up with WB-MRI is recommended for patients with MLS because of the potential for late relapse.

Off therapy surveillance

- In absence of supporting data, a pragmatic follow-up schedule for similar histologies with risk of later relapse (e.g. ASPS) would be every six months during the third, fourth and fifth year and then once yearly up to 10 years after diagnosis.

Ultrasonographic Findings

- Grayscale ultrasound
  - Firm mass of variable internal echogenicity
  - Typically of intermediate- or low-level echoes
  - Rarely anechoic with posterior acoustic enhancement & compressibility → favors benign, fluid-filled process
  - Must look closely for solid nodular components
- Color Doppler
  - Variable internal vascularity
  - Frequently only mild to intermediate
  - Check for spectral waveforms to confirm true flow

MR Findings

- T1: Typically similar to muscle signal intensity ± bright foci of hemorrhage
- T2 FS/STIR: Relatively uniform intermediate to bright signal intensity of solid tissue ± cystic/necrotic foci of very bright signal;
  - purely cystic appearance is uncommon (but still requires contrast)
  - Typically lacks significant surrounding muscle edema
- T1 C+ FS: Wide range of enhancement patterns
  - Often intermediate- to low-level enhancement ± nonenhancing foci of necrosis or hemorrhage
- DWI: Highly cellular tumors show restricted diffusion, typically with ADC values < 1.0×10^{-3} mm/s^2

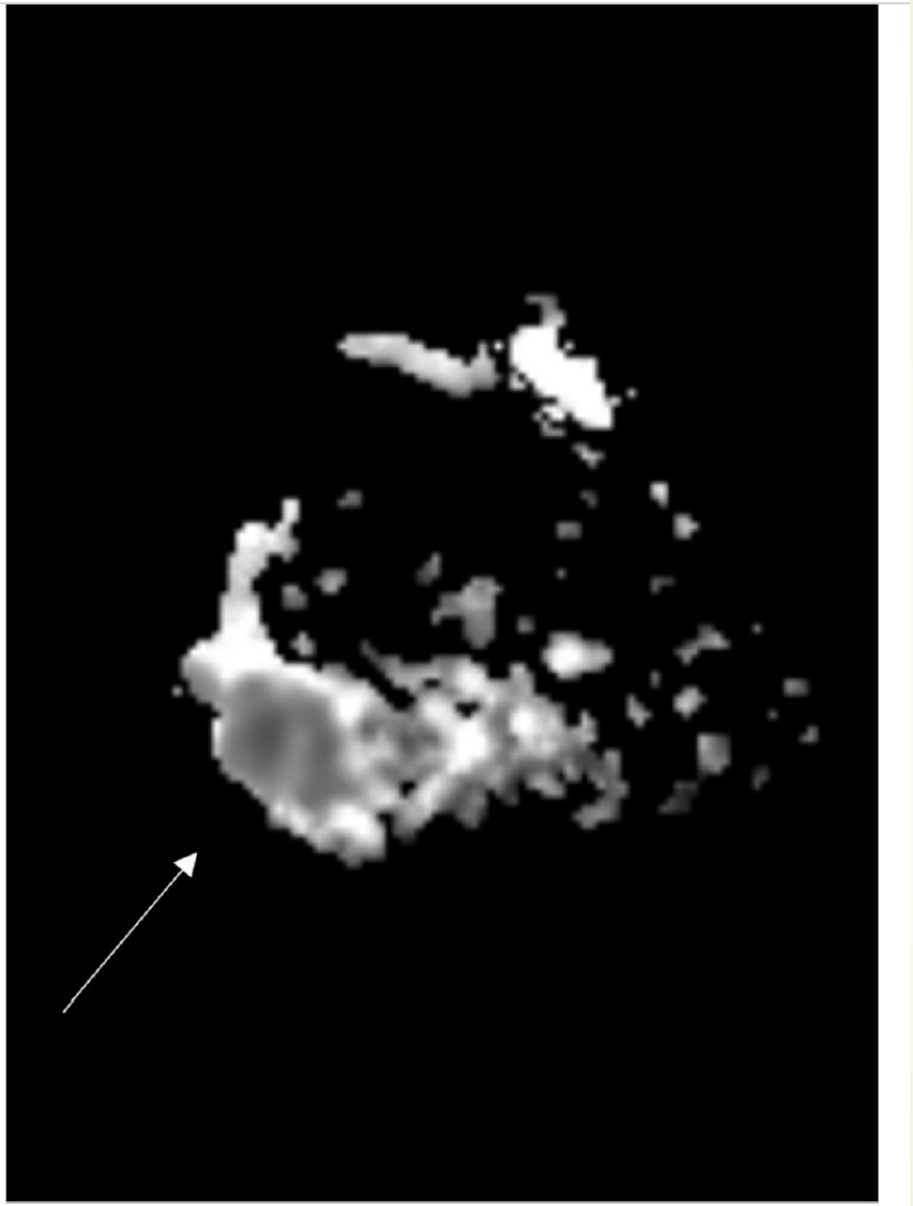


Fig. 2. Apparent Diffusion Coefficient (ADC) map (b value: 1000) demonstrates restricted diffusion within the lesion.

Imaging Recommendations

- Best imaging tool
  - MR ± IV contrast: Best study to characterize mass, determine local extent, & follow local response during/after therapy

- Protocol advice
  - MR technique
  - T1 sequence in at least 1 plane
  - Axial images show relationship of mass to neurovascular bundle (normally encased by fat)
  - Additional T1 FS sequence may help evaluate etiologies of bright signal in mass & determine true enhancement after contrast administration
  - Multiplanar fluid-sensitive T2 FS or STIR sequences to highlight most pathologies
  - Contrast is critical for showing solid vs. necrotic foci
  - Subtraction of precontrast images is most accurate

Pediatric Soft Tissue Malignancies

Tumor	Characteristic Imaging Features	Clinical Features	Prognosis
Rhabdomyosarcoma	Typical soft tissue sarcoma without specific features: Well-circumscribed, round/ovoid solid mass of intermediate/high T2 MR signal intensity with diffusion restriction & variable enhancement	Peak incidence overall: 2-6 years old; head/neck & genitourinary sites are more common than extremities; metastases in 15-20% at presentation	Overall 5-year survival: ~70%
Synovial sarcoma	30% show Ca^{2+}; often cystic-appearing; enhances with IV contrast; T2 MR triple sign (of intensities) is not specific; fluid-fluid levels in up to 25%; contiguity with bone is more common than remodeling or invasion	30% < 20 years old with median of 13-14 years in children; lower extremity is most common, often near joint (rarely in joint); slow growth is common	5-year survival: 36-76%; late recurrence is common
Extraskeletal Ewing sarcoma/PNET	No specific features overall; aggressive chest wall mass (Askin tumor) with pleural effusion & rib destruction is very suggestive	10-30 years old; most common in White patients; extraskeletal is less common than skeletal	Overall 5-year survival: ~ 61%
Infantile fibrosarcoma	Frequently infiltrative; often contains prominent cystic spaces; may be highly vascular	0-2 years old; 30-80% detected by/at birth; rapidly growing; skin involvement mimics vascular lesion; distal extremities are most common	5-year survival: 80% (better than adolescent/adult fibrosarcoma)
Undifferentiated sarcoma	No specific features	Multiple subtypes within this group	Varies by type, grade, stage
Extrarenal malignant rhabdoid tumor	No specific features overall; reported in virtually all anatomic sites (head/neck, trunk/viscera, limbs)	Older than renal rhabdoid patients with median < 4 years; ± concomitant CNS or renal rhabdoid tumors	5-year survival: 25-50%
MPNST	Features that can help distinguish from PN: Enlarging mass (> 5 cm) amidst stable PNs, loss of target sign on MR, ↑ activity on PET	~ 50% in neurofibromatosis type 1: 8-13% lifetime risk of MPNST	5-year survival: 23-69%

Dermatofibrosarcoma protuberans	Nodular, superficial mass with cutaneous elongation ± satellite nodules	Slow-growing, discolored skin mass	5-year survival: > 99%
Granulocytic/myeloid sarcoma (chloroma)	Background of diffuse marrow abnormalities	Acute myelogenous leukemia	5-year survival: 20-25%
Neuroblastoma	Typically small cutaneous & subcutaneous masses; ± discrete paraspinal primary mass; ± extensive marrow abnormalities	Wide range of clinical presentations; soft tissue metastases are most common < 18 months of age	Excellent in infant with metastases limited to liver, skin, & bone marrow; otherwise variable
Alveolar soft part sarcoma	Often brighter than muscle on T1 MR; typically shows prominent intra- & peritumoral vascularity, central necrosis, & infiltration	Head/neck is most common in children	5-year survival: 56-70%
Epithelioid sarcoma	Ca^{2+} in 20-30%; may have moderate surrounding edema with extension along fascia & tendon sheaths (uncommon for other sarcomas)	75% are 10-39 years old; distal upper extremity is most common, slow growth is frequent; proximal type is more aggressive	5-year survival: 50-70%
Angiosarcoma	Evidence of prior hemorrhage; tangles of high-flow vessels are uncommon	Typically de novo; rarely arise from preexisting vascular malformation	5-year survival: As low as 15%
Liposarcoma	Fat-poor myxoid subtype in 2nd decade of life	Extremely uncommon < 8-10 years old	Better than adult types

PNET = primitive neuroectodermal tumor; PN = plexiform neurofibroma; MPNST = malignant peripheral nerve sheath tumor.

DIFFERENTIAL DIAGNOSIS

Vascular Anomalies

- Infantile hemangioma
- Venous malformation
- Lymphatic malformation

Benign Fibrous/Fibrohistiocytic Tumors

- Fibrous hamartoma of infancy
- Myofibroma/myofibromatosis
- Nodular fasciitis
- Fibromatosis

Neurogenic Tumors

- Plexiform, localized, or diffuse neurofibroma
- Schwannoma

Fat-Containing Neoplasms

- Lipoma
- Lipoblastoma
- Hibernoma

Periarticular Cysts

- Ganglion vs. synovial or parameniscal cysts

Infectious/Inflammatory Masses

- Granuloma annulare
- Abscess

Posttraumatic Lesions

- Myositis ossificans
- Fat trauma/necrosis
- Hematoma

DIAGNOSTIC CHECKLIST

- **Consider**

• Benign & malignant soft tissue masses overlap in appearances; biopsy is often required

• Correlation with clinical history is important

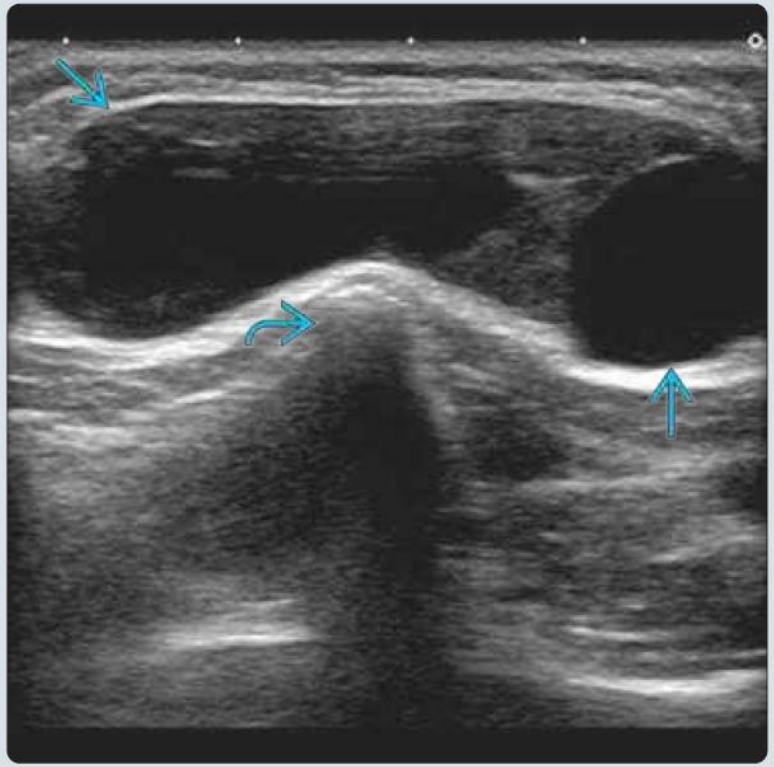
- Inflammatory & posttraumatic etiologies should be considered when pain & surrounding edema are present
- Firm & painless or mildly tender mass is more concerning
- Indolent growth does not exclude malignancy

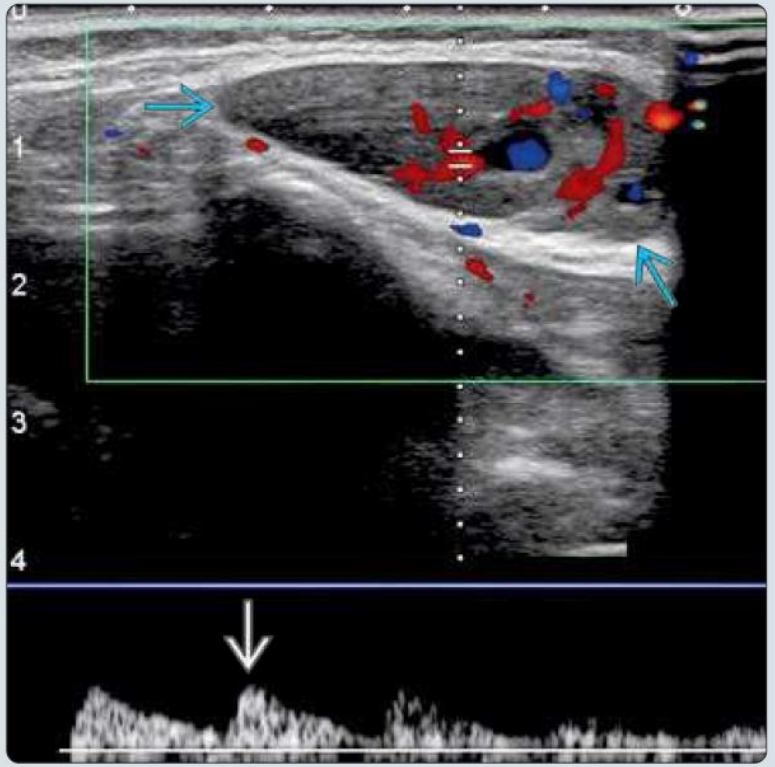
- **Image Interpretation Pearls**

• Soft tissue sarcomas often show well-defined margins

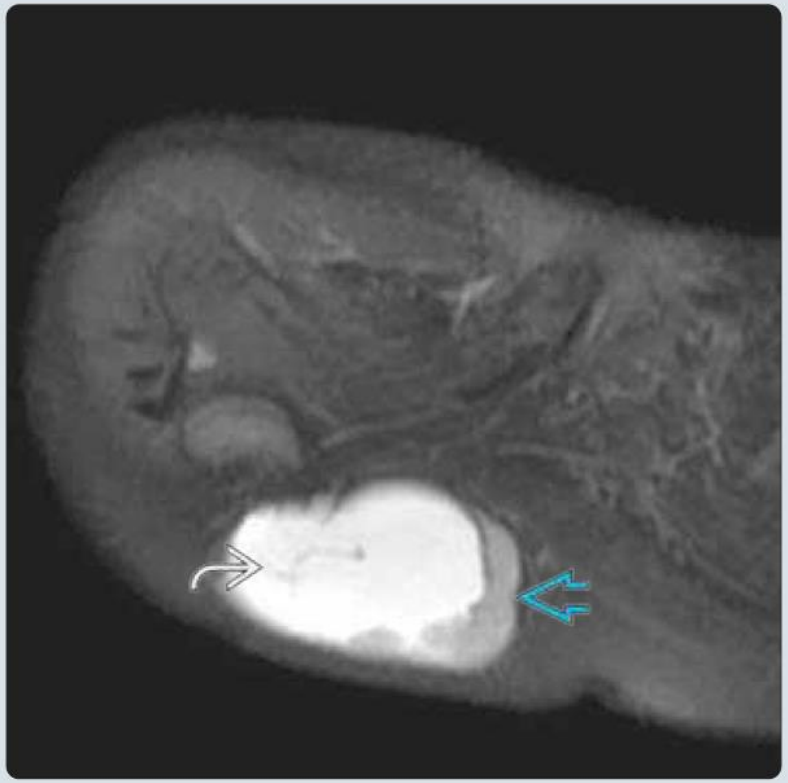
- Significant surrounding edema favors (but does not confirm) infectious/inflammatory or posttraumatic etiology; consider close follow-up before biopsy

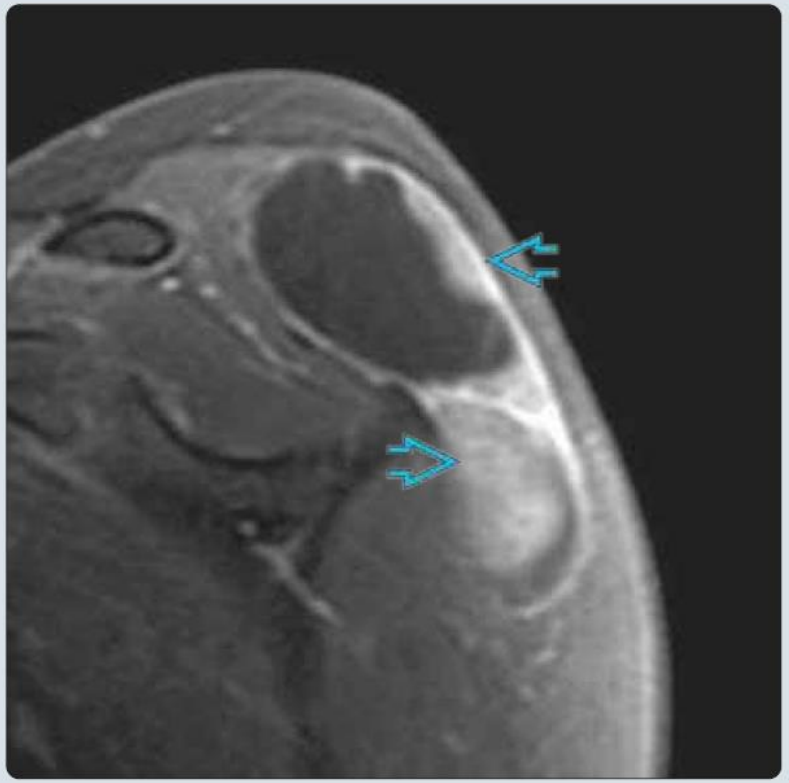
(Left) *Longitudinal ultrasound through a firm mass in the posterior right shoulder of a 5-year-old shows a mixed cystic & solid lesion ⇨ overlying the scapula ⇗. (Right) Transverse pulsed Doppler ultrasound in the same patient shows a moderate amount of internal vascularity throughout the solid portions of the lesion ⇨, including several arterial waveforms ➡. Spectral tracings (at several locations) are critical for characterizing flow within a lesion.*

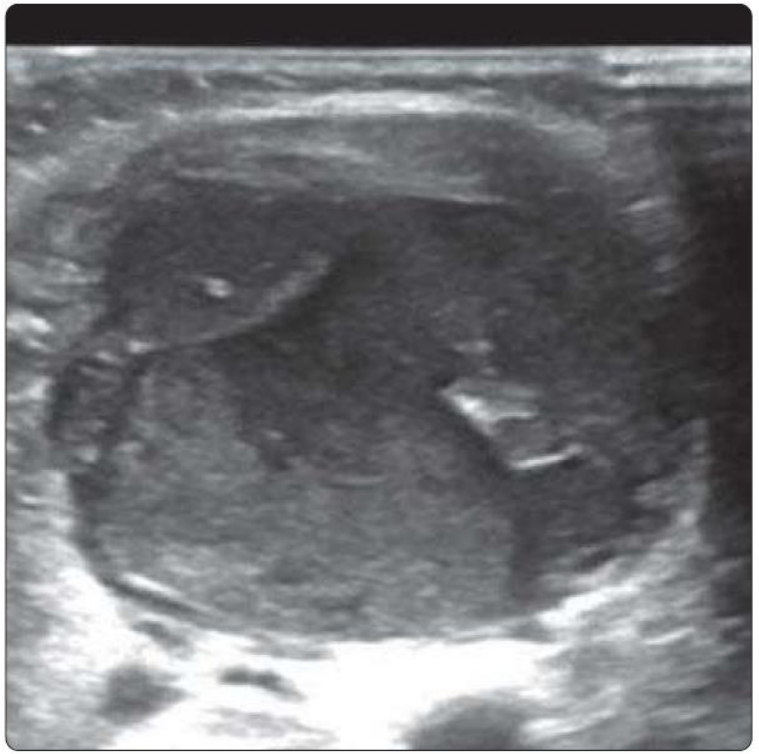


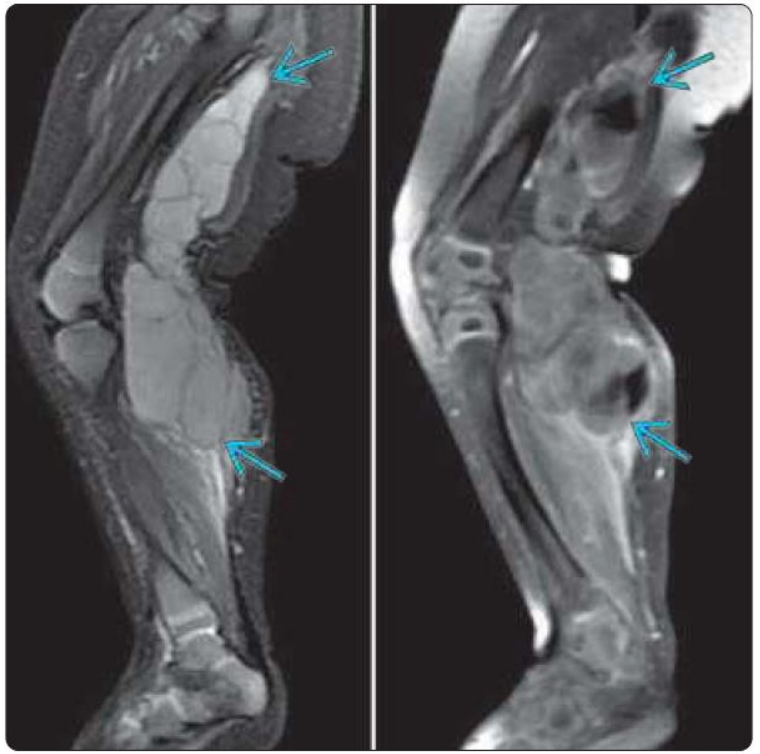


(Left) *Axial T2 FS MR in the same patient shows nodular intermediate signal intensity components along the wall of the mass. Some of the cystic portions show thin internal septations.* **(Right)** *Sagittal T1 C+ FS MR in the same patient shows enhancement of the solid components of the mass. While some of the cystic features could be seen in a lymphatic malformation, the enhancing, solid components are concerning for malignancy. An extraskeletal Ewing sarcoma was confirmed with biopsy.*









(Left) *Transverse ultrasound of the posterior calf in a 2-year-old girl with a palpable mass shows a well-circumscribed, heterogeneous, solid mass that was noncompressible. Internal vascularity was seen on Doppler (not shown).* **(Right)** *Sagittal T2 FS (left) & T1 C+ FS (right) MR images in the same patient demonstrate the full extent of the soft tissue mass ⇨ extending from the posterior upper thigh to the midleg. Biopsy showed an undifferentiated round cell sarcoma.*

BX

Indications

Image-guided biopsy (most often core needle biopsy) is recommended when:

- To determine whether a mass is benign or malignant.
- To obtain tissue for **histology, immunohistochemistry, cytogenetic, or molecular testing** (important for NRSTS classification).
- To collect samples for **microbiological studies** in suspected infection.
- For **staging purposes** (assessing local spread or metastasis).
- To confirm a diagnosis in cases where imaging is inconclusive.
- To guide treatment decisions (chemotherapy, radiotherapy, surgery).
- To target **viable tumor areas** (avoiding necrotic/cystic tissue) using CT, US, or MRI guidance.

Contraindications

There are no absolute contraindications, but several **relative ones**:

- **Uncorrectable coagulopathy** (e.g., high INR, severe thrombocytopenia).
- **Patient unable to cooperate** or maintain safe positioning.
- **Allergy or adverse reaction** to local anesthetics or sedatives required for the procedure.
- **Unsafe biopsy path** (must avoid major vessels, nerves, or compartments at risk of contamination).
- Performing biopsy **before adequate imaging**, which can cause artifacts and complicate interpretation.
- Targeting **necrotic/cystic areas** (leads to non-diagnostic results).
- Risk of **hematoma formation**, which may complicate later surgery or radiotherapy.
- Risk of **tumor cell seeding along the biopsy tract** → reason why biopsy tract should always be planned so it can be excised during definitive surgery.